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MAMMALIAN TOXICOLOGICAL EVALUATION OF DIMP AND DCPD.(U)  
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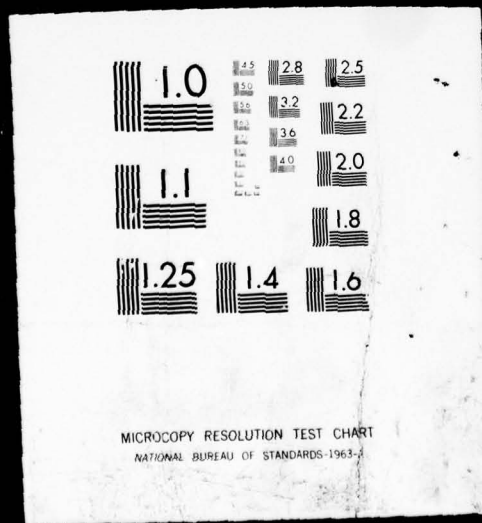
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(10) By  
E. Ross Hart, Ph.D.  
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A administration for 90 days to rats at levels up to 3000 ppm or to mice at levels up to 2100 ppm. At 1500 ppm dogs were not affected in 14 days. DIMP appeared to induce liver enzyme activity as manifest by diminished response to hexobarbital. It was reasonably well absorbed following oral administration, widely distributed and excreted, primarily in the urine, both unchanged and as two metabolites in rodents and three in dogs.

DCPD had oral LD50's of 520 and 378 mg/kg in male and female rats, respectively, and of 190 and 250 mg/kg in male and female mice. It produced conjunctival irritation when applied to rabbit eyes. It was minimally irritant to rabbit skin and did not produce evidence of systemic toxicity when so applied. It was not a sensitizer in guinea pigs. No evidence of toxicity followed its dietary administration for 90 days to rats at levels up to 750 ppm or to mice at levels up to 273 ppm. At 375 ppm dogs were not affected in 14 days. DCPD did not appear to induce liver enzyme activity as manifested by altered response to hexobarbital. It was absorbed following oral administration to mice, rats or dogs. It was widely distributed at 1 to 2 hours in all 3 species and excreted primarily in the urine as three metabolites in rats and two in mice and dogs.

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## EXECUTIVE SUMMARY

### DIMP

The oral LD50 values of DIMP were calculated to be 1125 and 826 (747-914) mg/kg in male and female rats, respectively, and 1041 (903-1201) and 1363 (1165-1594) mg/kg in male and female mice, respectively.

No evidence of toxicity resulted from dietary administration of DIMP to rats at levels of 300, 1000, and 3000 ppm for 90 days or to mice at levels of 210, 700, and 2100 ppm for 90 days.

Feeding of DIMP to male and female dogs for 14 days at 150, 500, and 1500 ppm did not lead to development of evidence of toxicity.

The Draize Eye Irritation Test revealed significant signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Some irritation occurred in spite of irrigation two or four seconds after the application, but only in the absence of irrigation was its degree important. In all but one case the irritation had cleared by the seventh day postexposure. That one was clear on Day 8.

Application of DIMP to the intact and abraded skin at doses of 0.2, 0.63, and 2.0 g/kg produced only minimal skin irritation. Death occurred in 3/4 at the highest dosage and in 1/4 at the intermediate dosage.

The test material, DIMP, was administered orally to rats at 3000 ppm in the diet for 4 days. The duration of hexobarbital-induced sleeping time measured on the 5th day was larger in control than in DIMP treated rats. Body weights and liver weights were not altered by treatment with DIMP. It was concluded that DIMP was a liver enzyme inducing agent.

DIMP should not be considered a strong sensitizer in guinea pigs.

DIMP was absorbed following oral administration to mice, rats, and dogs. Peak plasma levels occurred in 15 minutes in mice and in two hours in rats and dogs. Storage of DIMP was found in the skin of mice and rats at 72 hours and in the gall bladder of dogs. Excretion appeared to be primarily via the urine in all three species,

but there was some indication of biliary excretion in dogs. Eighty-five to 100% of the administered radioactivity appeared in urine and feces within 24 hours in all three species. Some 1 to 3% of the radioactivity in the urine was in the form of DIMP. The remainder appeared to be in the form of one major metabolite, in all three species. This metabolite was more polar than DIMP and was not conjugated.

#### DCPD

The oral LD50 values of DCPD were calculated to be 520 (420-645) and 378 (303-473) mg/kg in male and female rats, respectively, and 190 (125-289) and 250 (170-368) mg/kg in male and female mice, respectively.

No evidence of toxicity resulted from dietary administration of DCPD to rats at levels of 80, 250, and 750 ppm for 90 days or to mice at levels of 28, 91, and 273 ppm for 90 days.

Feeding of DCPD to male and female dogs for 14 days at 40, 125, and 375 ppm in the diet did not lead to development of evidence of toxicity.

The Draize Eye Irritation Test revealed signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Irritation was limited to the conjunctive, but occurred in spite of irrigation at two or four seconds after the application. In all cases, the irritation was absent by Day 3.

Application of DCPD to the intact and abraded skin at doses as high as 2.0 g/kg produced only minimal skin irritation and no signs of systemic intoxication.

The test material, DCPD, was administered orally to rats at a dietary level of 750 ppm for 4 days. The duration of hexobarbital-induced sleeping time measured on the 5th day was comparable in control and in DCPD treated rats. Body weights and liver weights were not altered by treatment with DCPD. It was concluded that DCPD was not a liver enzyme inducing agent.

DCPD is not a sensitizer in guinea pigs.

DCPD was absorbed after oral administration to mice, rats, and dogs. Peak plasma levels occurred in 2 hours in mice and dogs, and in 6 hours in rats. DCPD was widely distributed in all three species at 1 to 2 hours with the highest levels in urinary bladder, gall bladder

78 08 29 076  
2

and body fat in mice, in gall bladder and bile in dogs, and in body fat, adrenals and urinary bladder in rats. Excretion appeared to be primarily via the urine in all three species. About 85% of the administered radioactivity was accounted for in urine and feces within 24 hours. Urine from mice and dogs showed two radioactive components while rat urine also contained a third. All of these seemed to differ from DCPD on TLC, but none has yet been identified.

## FOREWORD

By agreement with the project officer for the US Army Medical Bioengineering Research and Development Laboratory, this report does not include the results of mutagenesis or demyelination tests. Several considerations, most important being impurities in the samples of diisopropyl methylphosphonate and dicyclopentadiene provided to Litton Bionetics, Inc. for mutagenesis testing, make interpretation of the results ambiguous. Mutagenesis tests have been repeated using highly purified samples of both compounds and will be reported under Contract DAMD17-77-C-7003.

Because results of the demyelination test with diisopropyl methylphosphonate were also ambiguous, Litton Bionetics, Inc. has repeated the test after thoroughly researching the method, and results of the follow-up study will also be reported under the latter contract.

In conducting the research described in this report, the investigator(s) adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences-National Research Council.

The method of euthanasia consisted of overdosage with carbon dioxide by inhalation in the case of group sacrifices or overdosage of pentobarbital sodium intraperitoneally or intravenously when one or a few individuals were sacrificed at a given time.

PART I - SECTION A

INTRODUCTION AND MATERIAL

DIMP

1. INTRODUCTION

The toxicity of DIMP has been studied acutely by the oral, dermal, and eye exposure routes in laboratory animals as well as in repeated subchronic exposure in rats, mice, and dogs. Special studies on liver enzyme induction activity, mutagenesis, and neurotoxicity have also been conducted. From the information gathered, dosages can be set for evaluation of DIMP in chronic studies.

Preliminary information on the rate of absorption, distribution, and excretion has been gained from pharmacokinetic studies. This can be used as background for the further evaluation of metabolic fate. The pharmacokinetic studies together with the toxicity work can form an understanding of the safe use and risk of DIMP with respect to human exposure.

2. MATERIAL

DIMP (Diisopropylmethylphosphonate) was obtained as a custom synthesis from Richmond Organics, 7342 Forest Hill Avenue, Richmond, Virginia 23225. Three separate orders were placed and three shipments were received and designated as follows:

<u>Receipt Date</u>	<u>Quantity</u>	<u>LBI No.</u>
8/5/75	500 g	755A
12/15/75	500 g	776A
2/16/76	500 g	781A

DIMP was analyzed using an OV-17/Reoplex 400 column as described in the procedure for analysis of DIMP in water samples used by Shell Chemical Company and the Colorado Department of Health. DIMP had a retention time of 6.2 minutes. Two impurities were observed, one at 5.2 minutes and the other at 11.8 minutes. Content was calculated on a total peak area basis.

<u>LBI No.</u>	<u>DIMP</u>	<u>Impurity</u>	
		<u>#1</u>	<u>#2</u>
755A	95.2%	3.1%	1.7%
776A	89.6%	5.6%	4.8%
781A	88.0%	6.7%	5.3%

## 2. MATERIAL (Continued)

Because of poor water solubility, solutions were prepared for administration to animals by dissolving DIMP in polyethylene glycol 400 (PEG 400) "Carbowax" obtained from Fisher Scientific Company.

PART I - SECTION B  
ACUTE ORAL TOXICITY STUDY IN RATS

DIMP

LBI PROJECT NO. 2558

SUMMARY

The oral LD50 values of DIMP were calculated to be 1125 and 826 (747-914) mg/kg in male and female rats, respectively.

1. OBJECTIVE

The objective of this study was to evaluate the acute toxicity of DIMP when administered orally to rats.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Sprague-Dawley rats were received from ARS/Sprague-Dawley, Madison, Wisconsin. These test animals were housed individually in hanging wire cages and acclimated to laboratory conditions. Water and Purina Laboratory Chow (ground) were provided ad libitum with the exception of the night before treatment when the food was removed from the cages.

Single graded doses of the test material, DIMP, dissolved in polyethylene glycol 400 (PEG 400) at a concentration of 195.2 mg/ml, were administered by gastric intubation to the test animals. Following treatment, the animals were observed frequently on the day of treatment and daily thereafter.

The animals were weighed on the day of treatment, and on Days 7 and 14 following treatment. Gross necropsies were performed on all animals that died during the study and on the surviving animals that were killed 14 days after treatment.

#### 4. RESULTS

The data have been summarized as follows:

<u>Dose</u> (mg/kg)	<u>Deaths</u> <u>Day</u>					<u>Total</u> <u>Mortality</u> <u>Deaths/Treated</u>
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5-14</u>	
<u>MALES</u>						
430	0	0	0	0	0	0/10
632	0	0	0	0	0	0/10
928	0	0	0	0	0	0/10
1362	10	0	0	0	0	10/10
2000	9	1	0	0	0	10/10
<u>FEMALES</u>						
430	0	0	0	0	0	0/10
632	0	0	0	0	0	0/10
928	5	3	0	0	0	8/10
1362	10	0	0	0	0	10/10
2000	9	1	0	0	0	10/10

The LD50 values (and 95% confidence limits) calculated by the method of Horn (Biometrics, 12:311, 1956) were 1125 mg/kg for male (the data do not permit calculation of confidence limits) and 826 (747-914) mg/kg for female rats, respectively.

Signs of intoxication in both males and females included decreased activity, occasional ataxia and prostration within one to four hours after dosing.

At necropsy of the survivors, all tissues appeared normal. Necropsy findings in animals of all levels dying during the study included hyperemia of the lungs, but most showed no abnormalities.

#### 5. CONCLUSIONS

Following the oral administration of graded doses of DIMP to fasted male and female rats, the LD50 values were 1125 and 826 (747-914) for males and females, respectively.

PART I - SECTION C  
ACUTE ORAL TOXICITY STUDY IN MICE

DIMP

LBI PROJECT NO. 2559

SUMMARY

The oral LD50 values of DIMP were calculated to be 1041 (903-1201) and 1363 (1165-1594) mg/kg in male and female mice, respectively.

1. OBJECTIVE

The objective of this study was to evaluate the acute toxicity of DIMP when administered orally to mice.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Swiss Webster mice were received from Camm Research, Wayne, New Jersey. These test animals were housed in groups of five by sex in solid bottom plastic cages and acclimated to laboratory conditions. Water and Purina Laboratory Chow (ground) were provided ad libitum with the exception of the night before treatment when the food was removed from the cages.

Single graded doses of the test material, DIMP, dissolved in Polyethylene Glycol 400 (PEG 400) at a concentration of 58.56 mg/ml, were administered by gastric intubation to the test animals. Following treatment, the animals were observed frequently on the day of treatment and daily thereafter.

The animals were weighed on the day of treatment, and on Days 7 and 14 following treatment. Gross necropsies were performed on all animals that died during the study and on the surviving animals that were killed 14 days after treatment.

#### 4. RESULTS

The data have been summarized as follows:

<u>Dose</u> (mg/kg)	<u>Deaths</u>					<u>Total</u>
	<u>Day</u>					<u>Mortality</u>
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5-14</u>	<u>Deaths/Treated</u>
<u>MALES</u>						
430	0	0	0	0	0	0/10
632	0	0	0	0	0	0/10
928	1	0	0	0	2	3/10
1362	9	0	0	0	0	9/10
2000	10	0	0	0	0	10/10
<u>FEMALES</u>						
430	0	1	0	0	1	2/10
632	0	0	0	0	0	0/10
928	2	0	0	0	0	2/10
1362	3	0	0	0	0	3/10
2000	10	0	0	0	0	10/10

The LD50 values (and 95% confidence limits) calculated by the method of Horn (Biometrics, 12:311, 1956) were 1041 (903-1201) and 1363 (1165-1594) mg/kg for male and female mice, respectively.

Signs of intoxication included decreased activity and prostration within one to four hours after dosing.

At necropsy of the survivors, all tissues appeared normal. Necropsy of animals of all levels dying during the study revealed nothing attributable to the treatment.

#### 5. CONCLUSION

Following the oral administration of graded doses of DIMP to fasted male and female mice, the LD50 values were 1041 (903-1201) and 1363 (1165-1594) for males and females, respectively.

PART I - SECTION D  
90-DAY TOXICITY STUDY IN RATS

DIMP

LBI PROJECT NO. 2563

SUMMARY

No evidence of toxicity resulted from dietary administration of DIMP to rats at levels of 300, 1000, and 3000 ppm for 90 days.

1. OBJECTIVE

The purpose of this study was to characterize the subchronic toxicity of DIMP by administration in the diet of rats over a 90-day period.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in rats obtained from ARS/Sprague-Dawley, Madison, Wisconsin, with body weights averaging 83.6 grams for males and 84.1 grams for females at initiation.

B. Animal Groups

The rats were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	32	32	Zero - Control
2	32	32	Low - 300 ppm
3	32	32	Medium - 1000 ppm
4	32	32	High - 3000 ppm

C. Diet Preparation

The rats were fed Purina Rat Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

### 3. EXPERIMENTAL DESIGN (Continued)

#### D. Observations

Body weights and food consumption were recorded weekly. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects. Entries were made in records only when abnormalities were noted.

#### E. Special Examinations

Ophthalmoscopic examination of each animal was performed by an experienced veterinarian before compound administration was begun and again during the final week of the study.

#### F. Clinical Laboratory Measurements

The following determinations were made on five rats of each sex from the control and each test level:

	<u>4 Wks</u>	<u>13 Wks</u>
<u>Hematocytology:</u>		
Erythrocyte count	x	x
Packed cell volume	x	x
Hemoglobin	x	x
Leukocyte count	x	x
Differential leukocyte count	x	x
<u>Blood Biochemistry:</u>		
Glucose	x	x
BUN	x	x
SGOT	x	x
Alkaline phosphatase	x	x
SGPT	-	x
Sodium	-	x
Potassium	-	x
Chloride	-	x
<u>Acetylcholinesterase:</u>		
Cells and plasma	x	x
Brain	-	x

### 3. EXPERIMENTAL DESIGN (Continued)

#### F. Clinical Laboratory Measurements

	<u>4 Wks</u>	<u>13 Wks</u>
<u>Urinalysis:</u>		
Color	x	x
Specific gravity	x	x
pH	x	x
Sugar	x	x
Protein (albumin)	x	x
Ketones (acetone)	x	x
Microscopic examination of sediment	x	x

#### G. Terminations

All survivors were killed after 13 weeks. The planned 2 and 4 week recovery period was eliminated by agreement with the Project Officer since no effects had been seen.

#### H. Postmortem Examinations

Each animal was subjected to a gross necropsy and any observed abnormalities were recorded. The organs listed below were weighed.

kidney	heart	adrenals (after fixation)
liver	gonads	thyroid (after fixation)
spleen	brain	

Generous samples of each of the following were collected and held frozen for chemical analysis as indicators of tissue storage:

liver	brain	eye
kidneys	skeletal	testes
body fat	muscle	

Suitable samples of the following organs were preserved in 10% neutral formalin:

thyroid	small intestine	seminal vesicles
lung	large intestine	bone marrow
heart	kidneys	brain
mesenteric lymph node	adrenal glands	pituitary
liver	urinary bladder	thoracic spinal cord
spleen	testes with epididymis	rib junction
pancreas	or ovary	eye
stomach	uterus/prostate	nerve with muscle
		any unusual lesions

### 3. EXPERIMENTAL DESIGN (Continued)

#### I. Histopathologic Examination

The following tissues were examined microscopically from five male and five female rats in the control and high level test groups:

thyroid	small intestine	seminal vesicles
lung	large intestine	bone marrow
heart	kidneys	brain
mesenteric lymph	adrenal glands	pituitary
node	urinary bladder	thoracic spinal cord
liver	testes with epididymis	rib junction
spleen	or ovary	eye
pancreas	uterus/prostate	nerve with muscle
stomach		any unusual lesions

### 4. RESULTS

#### A. Drug Administration

No difficulty was encountered with the preparation of the diets according to plan or with their acceptance by the rats.

#### B. Observations

One control male died in the ninth week, one low dose male was found dead on the day it was scheduled for sacrifice, and two high dose males were found dead--one in the tenth and one in the twelfth week. All females survived. The average values for body weights for each of the various groups are presented in Table I-D-1.

The occasional significant differences between control and treated groups are scattered and show no relationship to dosage or duration of treatment. They are judged to be of no toxicologic importance. Food consumption values are presented similarly in Table I-D-2. No important differences from controls were seen in either sex at any dosage. Other signs of toxicity were not noted.

#### C. Special Examinations

Ophthalmoscopic examinations during the week before termination revealed a total of 12 rats with some opacity of the lens. Incidence ranged from 2 to 5 per sex/dose group of 32. Discussion with a veterinary ophthalmologist elicited the opinion that this can be considered normal. This is not believed to be an important finding, but warrants attention in longer term studies.

#### 4. RESULTS (Continued)

##### D. Clinical Laboratory Measurements

The observed values for hematocytology at the four-week interval and at termination are presented in Table I-D-3. Only group means and standard errors are presented. Differential white cell counts are not analyzed statistically. The few instances of statistically significant differences from corresponding controls are so scattered as to be of no toxicologic importance.

The recorded values for various blood biochemistry measures at the four-week interval and at termination are tabulated in Table I-D-4. There are instances of statistically significant differences from control but they are judged to be of no toxicologic importance.

Urinalysis values obtained at four weeks and at termination are presented in Table I-D-5. No important deviations from normal were noted.

RBC, plasma, and brain cholinesterase values are presented in Tables I-D-6 and I-D-7. No compound effect is apparent except in the plasma from females at 13 weeks where the control values are exceptionally high when compared to other intervals.

##### E. Recovery Phase

The two- and four-week recovery phases of the study proved to be noncontributing since no toxic effects developed, no "recovery" could be expected.

##### F. Postmortem Examination

The weights of various organs collected at terminal necropsy are presented in Table I-D-8 as recorded, and in Table I-D-9 calculated as percentages of body weight. Again no important differences were noted.

##### G. HISTOPATHOLOGIC EXAMINATION

The tissues listed in 3H above were processed in the conventional manner for preparation of sections stained with hematoxylin and eosin for examination of a staff pathologist. The pathologist's own summary is attached. No important abnormalities were noted.

#### 5. CONCLUSIONS

No evidence of toxicity resulted from dietary administration of DIMP to rats at levels of 300, 1000, and 3000 ppm for 90 days.

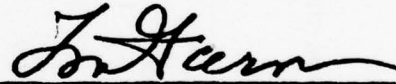
90-DAY TOXICITY STUDY IN RATS

DIMP

LBI PROJECT NO. 2563

PATHOLOGY SUMMARY

The microscopic lesions observed in this study were those routinely encountered in rats and mice. They appeared in all dosed groups and did not differ significantly from those seen in the controls.



F. M. Garner, D.V.M.

Veterinary Pathologist

Veterinary Sciences Division

TABLE I-D-1  
BODY WEIGHTS  
(kg)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

MALES  
DIMP

CONTRL	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	30	30	32	32	32	31	31	31	31	31	31	10	10	5
MEAN	80.7	136.2	171.8	210.4	251.8	281.7	298.9	311.9	323.7	330.0	339.2	345.9	355.3	364.0	364.8	372.0	355.5	363.9
S.E.	1.1	2.4	3.3	4.5	5.5	6.2	6.8	7.9	8.9	8.0	8.3	9.7	10.0	8.9	19.5	17.7	26.7	27.0

300 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	29	32	32	32	32	32	32	32	32	10	10	5	5
MEAN	82.4	134.2	164.3	212.0	252.0	284.4	300.8	318.9	328.6	344.0	351.1	356.5	361.2	369.6	352.3	357.3	322.6	328.6
S.E.	1.0	1.6	2.0	2.3	2.4	2.6	2.9	3.3	4.2	4.7	6.3	8.0	9.1	9.4	16.7	16.0	23.0	25.2
T	1.2	0.7	1.9	0.3	0.0	0.4	0.3	0.8	0.5	1.5	1.1	0.8	0.4	0.4	0.4	0.6	0.9	1.0

1000 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	29	32	32	32	32	32	32	32	31	10	10	5	5
MEAN	85.8	139.2	169.8	216.0	256.9	280.0	305.2	321.2	332.8	354.2	353.5	362.1	369.2	377.8	393.7	396.6	412.0	418.2
S.E.	1.1	1.7	2.1	3.1	3.9	4.6	5.0	5.0	6.1	7.0	7.5	7.8	7.9	5.8	10.4	10.7	12.0	12.5
T	3.3	1.0	0.5	1.0	0.8	0.2	0.7	1.0	0.8	2.3	1.3	1.3	1.1	1.3	1.3	1.2	1.9	1.8

3000 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	30	32	32	32	32	31	31	30	30	10	10	5	5
MEAN	85.5	139.5	170.6	222.2	261.6	257.6	306.4	319.3	329.8	334.0	341.8	349.2	352.6	359.4	353.8	356.9	355.0	358.3
S.E.	0.8	1.4	2.2	2.7	2.7	3.1	3.6	3.9	5.4	6.4	6.7	7.8	7.1	7.8	23.7	25.0	37.7	39.7
T	3.6	1.2	0.3	2.2	1.6	3.5	1.0	0.8	0.6	0.4	0.2	0.3	0.2	0.4	0.4	0.5	0.0	0.1

TABLE I-D-1 (Continued)

## BODY WEIGHTS

(kg)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

FEMALES

DIMP

		1/ 1	1/ 8	1/15	1/22	1/29	2/ 5	2/12	2/19	2/26	3/ 4	3/11	3/18	3/25	4/ 1	4/ 8	4/15	4/22	
CONTRAL		12/25	1/ 1	1/ 8	1/15	1/22	1/29	2/ 5	2/12	2/19	2/26	3/ 4	3/11	3/18	3/25	4/ 1	4/ 8 <td>4/15<td>4/22</td></td>	4/15 <td>4/22</td>	4/22
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	31	32	32	32	32	32	32	32	32	32	32	32	32	32
MEAN	83.7	124.2	143.8	159.6	179.6	191.8	199.9	207.5	210.4	215.5	220.7	225.0	227.7	229.3	237.5	241.7	244.2	243.8	
S.E.	2.3	1.9	1.4	1.7	1.6	1.8	2.1	2.0	2.0	2.3	2.3	2.3	2.1	2.2	5.1	3.8	6.3	6.6	
300 ppm		12/25	1/ 1	1/ 8	1/15	1/22	1/29	2/ 5	2/12	2/19	2/26	3/ 4	3/11	3/18	3/25	4/ 1	4/ 8 <td>4/15<td>4/22</td></td>	4/15 <td>4/22</td>	4/22
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	31	29	32	32	32	32	32	32	32	32	32	32	32	32
MEAN	86.3	128.3	139.6	162.8	178.9	188.4	189.2	206.8	209.2	215.9	218.9	221.6	221.6	225.7	228.4	235.6	239.2	235.1	238.9
S.E.	2.2	2.0	1.8	2.1	2.6	2.5	2.2	2.2	2.4	2.6	2.7	3.0	3.0	2.9	3.0	5.4	4.5	7.1	7.8
T	0.8	1.5	1.8	1.2	0.2	1.1	3.5	0.2	0.4	0.1	0.5	0.5	0.9	0.6	0.2	0.3	0.4	1.0	0.5
1000 ppm		12/25	1/ 1	1/ 8	1/15	1/22	1/29	2/ 5	2/12	2/19	2/26	3/ 4	3/11	3/18	3/25	4/ 1	4/ 8 <td>4/15<td>4/22</td></td>	4/15 <td>4/22</td>	4/22
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	31	31	29	32	32	32	32	32	32	32	32	32	32	32	32
MEAN	83.0	124.2	141.6	164.0	179.2	194.2	174.2	202.0	206.2	216.7	207.6	221.9	227.6	229.8	234.1	238.9	239.7	249.3	249.3
S.E.	2.3	2.2	1.3	1.6	1.9	2.5	2.5	2.2	3.2	2.6	2.7	2.8	3.1	3.4	3.5	8.6	6.9	8.6	9.6
T	0.2	0.0	1.2	1.9	0.2	5.7	5.7	0.7	0.3	1.9	2.3	0.3	0.7	0.5	1.2	0.1	0.3	0.5	0.5
3000 ppm		12/25	1/ 1	1/ 8	1/15	1/22	1/29	2/ 5	2/12	2/19	2/26	3/ 4	3/11	3/18	3/25	4/ 1	4/ 8 <td>4/15<td>4/22</td></td>	4/15 <td>4/22</td>	4/22
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	32	29	29	30	32	32	32	32	32	32	32	30	30	30	30	30
MEAN	83.5	124.1	142.5	165.2	181.7	191.9	191.9	200.0	209.2	220.5	222.7	226.2	228.4	231.8	225.7	228.9	231.7	238.9	242.8
S.E.	2.2	2.1	1.8	2.6	3.7	4.6	4.6	6.2	5.7	6.1	6.0	5.4	5.7	5.8	3.6	6.3	4.6	4.4	4.1
T	0.1	0.0	0.6	1.8	0.5	0.0	0.0	0.0	0.3	1.6	1.1	0.9	0.6	0.7	0.9	1.1	1.7	0.7	0.1

TABLE I-D-2

FOOD CONSUMPTION  
(Mean kg/day/rat)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

## MALES

## DIMP

WK NO.	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
SAMPLE	32	32	32	30	30	32	32	28	26	31	30	27	28	10	15	16	17
MEAN	16.9	19.1	21.3	23.1	24.8	25.0	22.7	20.8	21.1	22.2	21.9	21.8	23.3	22.6	23.4	22.8	20.8
S.E.	0.5	0.4	0.4	0.4	0.3	0.4	2.6	2.7	0.8	1.0	0.8	0.6	0.6	0.4	0.4	1.3	0.9

WK NO.	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
SAMPLE	32	32	32	31	29	32	32	26	26	30	29	27	26	10	9	4	5
MEAN	17.3	21.3	22.3	24.2	27.7	29.0	25.1	24.0	23.2	23.1	22.2	22.5	23.8	22.5	22.7	18.3	17.9
S.E.	0.5	0.3	0.3	0.5	1.6	1.5	2.1	0.6	0.8	0.8	1.0	5.4	6.6	1.4	1.7	0.4	0.3
T	0.6	4.0	2.1	1.9	1.9	2.7	1.0	2.2	2.0	0.7	0.2	0.5	0.4	0.1	0.5	2.8	3.0

WK NO.	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
SAMPLE	32	32	32	31	29	32	32	32	31	30	29	29	29	7	15	16	17
MEAN	10.0	20.5	21.1	23.0	25.4	25.0	23.9	22.4	21.1	22.2	22.0	22.6	23.0	21.8	23.8	23.9	22.1
S.E.	0.4	3.5	2.4	1.3	1.9	0.4	1.8	0.7	0.8	0.6	0.4	0.4	0.4	0.2	0.1	0.1	0.1
T	0.5	1.6	0.3	0.2	1.0	0.1	0.5	1.1	0.0	0.0	0.2	1.1	0.4	0.9	0.6	1.6	2.4

WK NO.	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
SAMPLE	32	30	32	31	30	32	32	31	31	31	31	28	29	9	10	5	5
MEAN	17.2	20.5	21.2	23.4	30.5	27.1	24.7	22.0	20.6	19.8	21.1	21.4	21.9	21.2	22.4	21.1	18.6
S.E.	0.4	0.3	0.3	0.3	1.4	4.9	1.6	0.7	0.9	0.7	0.7	1.7	5.1	0.4	2.8	0.3	0.3
T	0.5	2.9	0.3	0.6	3.9	1.1	0.9	0.8	0.4	2.0	0.7	0.3	1.0	1.4	0.8	1.5	2.2

TABLE I-D-2 (Continued)  
FOOD CONSUMPTION  
(Mean kg/day/rat)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

FEMALES

DIMP

	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	31	32	32	32	32	30	32	32	31	29	8	10	5	5
MEAN	16.3	17.8	18.2	18.4	19.6	22.6	19.5	19.1	18.5	19.1	17.8	18.5	18.4	16.7	18.3	22.2	19.5
S.E.	0.4	0.5	1.7	2.1	0.7	1.8	0.8	0.7	0.8	0.8	0.5	0.5	0.2	0.2	0.1	1.9	2.1

	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	31	29	32	32	32	32	32	32	32	31	10	10	5	5
MEAN	17.4	18.1	17.1	17.7	18.9	20.6	16.9	17.3	17.6	17.1	16.6	17.5	18.3	17.9	18.8	19.2	18.3
S.E.	0.7	0.4	0.3	0.5	0.5	0.4	2.8	2.2	1.5	1.4	0.3	0.3	0.3	0.2	0.2	0.1	0.2
T	1.4	0.6	1.5	1.3	0.8	1.1	2.4	1.7	0.8	1.8	2.1	1.7	0.3	2.5	1.3	3.0	1.1

	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	32	32	31	29	32	32	32	30	32	32	32	32	10	10	5	5
MEAN	15.8	17.0	17.1	17.4	22.1	19.3	17.8	17.3	18.9	16.4	16.6	17.2	18.7	16.9	17.3	18.4	15.9
S.E.	0.4	0.2	0.5	2.1	3.7	1.2	1.4	0.4	0.3	0.4	0.4	0.4	0.3	0.2	0.1	0.1	0.1
T	0.7	1.3	0.6	1.1	2.1	1.5	1.6	2.2	0.4	3.1	2.0	2.0	0.8	0.2	3.1	3.7	3.4

	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15	4/22
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	32	31	31	29	30	32	32	30	31	32	30	31	30	10	10	5	5
MEAN	16.1	16.5	15.8	16.9	18.3	21.4	18.0	16.9	17.5	16.0	16.6	17.1	17.7	16.1	17.3	18.5	16.9
S.E.	0.6	0.3	0.3	0.4	0.4	1.9	0.6	0.3	0.5	1.7	3.3	1.3	0.4	0.3	0.3	0.9	0.1
T	0.2	2.4	3.1	2.4	1.5	0.5	1.7	2.7	1.2	2.5	1.4	1.7	1.6	1.0	1.9	1.7	2.3

TABLE I-D-3  
HEMATOCYTOLOGY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm %</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	48.0	15.6	6.19	11.5
S.E.	1.4	0.86	0.32	0.93
<u>2 - 300 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.0	16.6	6.85	13.1
S.E.	0.75	0.43	0.21	0.58
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.4	6.76	12.1
S.E.	0.24	0.41	0.16	1.0
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	48.0	15.6	6.06	10.8
S.E.	1.2	0.56	0.28	1.3

TABLE I-D-3 (Continued)  
 HEMATOCYTOLOGY  
 GROUP MEANS AND STANDARD ERROR  
 13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm %</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.8	7.62	12.1
S.E.	1.0	0.33	0.31	1.8
<u>2 - 300 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	52.5	16.9	7.76	12.3
S.E.	0.93	0.64	0.39	2.3
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.0	16.8	7.53	11.3
S.E.	0.72	0.21	0.24	0.92
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	52.0	17.2	7.52	12.9
S.E.	2.3	0.68	0.24	1.7

TABLE I-D-3 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS AND STANDARD ERROR

4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm %</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	46.5	14.7	5.72	8.3
S.E.	1.8	0.58	0.46	1.3
<u>3 - 300 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	48.5	16.7	6.92	8.9
S.E.	1.1	0.43	0.18	1.5
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	47.5	16.1	6.43	6.8
S.E.	1.0	0.47	0.20	0.59
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	46.0	15.5	6.42	7.7
S.E.	1.4	0.44	0.14	0.71

TABLE I-D-3 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm %</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	47.0	15.7	7.04	9.1
S.E.	0.54	0.22	0.18	1.1
<u>2 - 300 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	48.5	16.3	7.15	8.6
S.E.	0.85	0.27	0.27	1.5
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.8	7.12	7.9
S.E.	1.4	0.40	0.35	0.59
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.6	6.92	8.6
S.E.	0.88	0.18	0.20	1.2

TABLE I-D-4  
BLOOD CHEMISTRY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN mg%</u>	<u>GLU- COSE mg%</u>	<u>ALK. PHOS. I.U.</u>	<u>SGPT I.U.</u>
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	18	79	168	16
S.E.	1.2	5.4	12	1.2
<u>2 - 300 ppm</u>				
NO. SAMPLES	5	5	3	3
MEAN	19	73	163	18
S.E.	0.73	6.8	6.5	0.85
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	20	79	177	15
S.E.	0.80	6.5	22	0.63
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	18	72	140	16
S.E.	0.51	3.0	11	0.92

TABLE I-D-4 (Continued)

## BLOOD CHEMISTRY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg %	<u>GLU- COSE</u> mg %	<u>ALK. PHOS.</u> I.U.	<u>SGOT</u> I.U.	<u>SGPT</u> I.U.	<u>Cl</u> mEq/L	<u>K</u> mEq/L	<u>Na</u> mEq/L
<u>MALES</u>								
<u>1 - CONTROL</u>								
NO. SAMPLES	5	5	5	5	5	1	5	5
MEAN	18	99	109	261	26	112	8.9	194
S.E.	0.87	6.2	14	19	2.2		0.86	7.8
<u>2 - 300 ppm</u>								
NO. SAMPLES	5	5	5	5	5	1	4	4
MEAN	23	97	239	239	30	110	8.1	192
S.E.	3.9	3.6	12	20	3.3		0.28	5.8
<u>3 - 1000 ppm</u>								
NO. SAMPLES	5	5	5	5	5	-	5	5
MEAN	21	103	116	263	30		8.3	194
S.E.	3.0	10	2.7	28	4.8		0.56	5.3
<u>4 - 3000 ppm</u>								
NO. SAMPLES	5	5	5	5	5	-	5	5
MEAN	19	102	130	245	24		10.5	196
S.E.	1.5	6.4	26	7.2	1.2		1.4	7.4

TABLE I-D-4 (Continued)

BLOOD CHEMISTRY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg%	<u>GLU- COSE</u> mg%	<u>ALK. PHOS.</u> I.U.	<u>SGPT</u> I.U.
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	19	83	97	15
S.E.	0.87	2.8	5.3	0.73
<u>2 - 300 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	20	84	86	15
S.E.	0.86	8.0	5.3	1.4
<u>3 - 1000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	21	90	95	13
S.E.	2.3	7.7	11	0.81
<u>4 - 3000 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	20	86	87	12
S.E.	1.5	5.5	14	0.68

TABLE I-D-4 (Continued)

## BLOOD CHEMISTRY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg %	<u>GLU- COSE</u> mg %	<u>ALK. PHOS.</u> I.U.	<u>SGOT</u> I.U.	<u>SGPT</u> I.U.	<u>Cl</u> mEq/L	<u>K</u> mEq/L	<u>Na</u> mEq/L
<u>FEMALES</u>								
<u>1 - CONTROL</u>								
NO. SAMPLES	5	5	5	5	5	1	4	4
MEAN	22	112	108	226	18	118	7.8	187
S.E.	1.2	6.6	13	11	0.45		0.67	8.3
<u>2 - 300 ppm</u>								
NO. SAMPLES	5	5	5	5	5	2	4	4
MEAN	21	110	80	236	17	123	7.7	186
S.E.	0.71	11	6.0	24	0.89	7.0	0.36	9.1
<u>3 - 1000 ppm</u>								
NO. SAMPLES	5	5	5	4	5	2	4	4
MEAN	18	93	78	228	20	112	7.4	180
S.E.	0.51	12	4.6	26	3.0	10	0.27	10
<u>4 - 3000 ppm</u>								
NO. SAMPLES	5	5	5	5	5	-	5	5
MEAN	21	107	68	229	20		8.8	194
S.E.	1.1	8.1	12	8.1	0.68		0.19	8.0

## URINALYSIS

### KEY

Color:    Y = Yellow  
          Or = Orange  
          Br = Brown  
          Str = Straw

Casts:    fgr = Finely Granular

Crystals: T.P. = Triple Phosphate  
          U.A. = Uric Acid  
          Ca O = Calcium Oxalate

- or 0 = None or Negative  
+ = Trace, Occasional, Rare,  
  Very Little  
1+ = Slight, Small, Little,  
     Few, Some, Light  
2+ = Moderate, Frequent, Large  
3+ = Severe, Heavy, Many  
4+ = Maximal  
TNTC = Too Numerous to Count

TABLE I-D-5  
URINALYSIS

4-WEEKS - DIMP - MALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL- BUMIN	GLU- COSE	KE- TONES	BILI- RUBIN	OCCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*										CRYSTALS		
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	T.P.	Ca	O. OTHER			
GROUP 1 - CONTROL																						
111248	Y	Hazy	1.040	7	3+	0	0	0	0	-	0-3	0-1	-	-	3+	-	3+	-	-			
111249	Y	Hazy	1.036	8	2+	0	0	0	0	0-1	0-2	0-1	-	-	4+	-	3+	-	-			
111250	Y	Hazy	1.031	9	+	0	0	0	0	0-1	-	0-1	-	1+	4+	-	3+	-	-			
111251	Y	Clear	1.046	5	2+	0	0	0	0	4-5	1-2	-	-	-	+	-	-	-	-			
111252	Y	Cloudy	1.022	9	+	0	0	0	0	1-2	0-1	1-2	-	-	4+	-	2+	-	-			
GROUP 2 - 300 ppm																						
111312	Y	Hazy	1.050	6	2+	0	0	0	0	0-1	0-1	0-1	-	2+	4+	-	-	-	-			
111313	Y	Hazy	1.034	8	2+	0	0	0	0	0-1	-	0-1	-	-	3+	-	3+	-	-			
111314	Y	Clear	1.052	5	1+	0	0	0	0	4-5	2-3	1+	-	-	-	-	1+	-	-			
111315	Y	Clear	1.062	5	1+	0	0	0	0	8-10	1-2	-	-	-	1+	-	-	-	-			
111316	Y	Cloudy	1.014	6	0	0	0	0	0	2-3	-	1-2	-	-	2+	-	-	-	-			
GROUP 3 - 1000 ppm																						
111376	Y	Cloudy	1.014	9	0	0	0	0	+	0-1	4-8	0-1	-	-	4+	-	3+	-	-			
111377	Y	Cloudy	1.070	7	4+	0	0	0	0	-	-	-	-	3+	4+	-	4+	-	-			
111378	Y	Clear	1.045	5	1+	0	0	0	0	3-4	1-2	4-5	-	-	1+	-	1+	-	-			
111379	Y	Clear	1.066	5	3+	0	0	0	0	7-8	0-1	+	-	-	-	-	-	-	-			
111380	Y	Clear	1.032	5	1+	0	0	0	0	3-4	1-2	-	-	-	1+	-	-	-	-			
GROUP 4 - 3000 ppm																						
111441	Y	Hazy	1.060	8	4+	0	0	0	0	15-20	-	4-8	-	2+	4+	-	2+	-	-			
111442	Y	Cloudy	1.026	9	1+	0	0	0	0	-	-	-	-	-	4+	-	4+	-	-			
111443	Y	Clear	1.060	5	2+	0	0	0	0	6-8	2-3	6-8	-	-	1+	-	-	-	-			
111444	Y	Clear	1.024	6	1+	0	0	0	0	3-4	-	1-2	-	-	1+	-	-	-	-			

\*Microscopic examination per high power field.

TABLE I-D-5 (Continued)

## URINALYSIS

13-WEEKS - DIMP - MALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	PH	AL- BUMIN	GLU- COSE	KE- TONES	BILLI- RUBIN	OCCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*									
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	CRYSTALS		
																	T.P.	Ca	OTHER
GROUP 1 - CONTROL																			
11256	Y	Hazy	1.033	7	2+	0	3+	0	0	0-1	-	-	-	1+	4+	-	4+	-	-
11258	Y	Hazy	1.031	7	3+	0	2+	0	0	-	-	-	-	1+	4+	-	4+	-	-
11259	Y	Clear	1.060	8	3+	0	2+	0	0	0-1	0-1	-	-	-	3+	-	3+	-	-
11260	Or	Hazy	1.100	5	4+	0	2+	0	0	0-3	0-1	2-5	-	2+	1+	-	-	1+	-
11261	Y	Hazy	1.065	6	2+	0	2+	0	0	0-1	0-1	-	-	1+	3+	-	3+	-	-
GROUP 2 - 300 ppm																			
11322	Y	Hazy	1.090	5	4+	0	1+	0	0	4-8	10-15	2-5	-	3+	2+	-	-	-	-
11323	Y	Cloudy	1.024	9	1+	0	0	0	0	-	-	-	-	-	4+	-	4+	-	-
11324	Or	Hazy	1.100	5	4+	0	2+	0	0	-	-	-	-	1+	1+	-	-	-	-
11325	Y	Hazy	1.045	8	3+	0	1+	0	0	4-8	-	-	-	-	4+	-	4+	-	-
GROUP 3 - 1000 ppm																			
11389	Y	Hazy	1.037	8	3+	0	3+	0	0	-	TNTC	-	-	-	4+	-	3+	-	-
11390	Y	Cloudy	1.055	8	2+	0	1+	0	0	-	-	-	-	2+	4+	-	3+	-	-
11391	Or	Hazy	1.100	5	4+	0	2+	0	0	-	-	-	-	2+	1+	-	3+	-	-
11392	Or	Hazy	1.055	5	1+	0	1+	0	0	-	-	-	-	1+	1+	-	-	-	-
11393	Y	Hazy	1.050	7	3+	0	1+	0	0	0-1	4-8	-	-	1+	4+	-	3+	-	-
GROUP 4 - 3000 ppm																			
11449	Y	Hazy	1.028	7	3+	0	1+	0	0	-	-	-	-	1+	4+	-	2+	-	-
11450	Y	Hazy	1.075	6	4+	0	2+	0	0	0-1	TNTC	0-1	-	-	-	-	-	1+	-
11451	Y	Hazy	1.055	8	3+	0	1+	0	0	0-3	TNTC	0-1	-	-	4+	-	3+	-	-
11453	Or	Hazy	1.100	5	4+	0	1+	0	0	0-3	0-1	-	-	2+	3+	-	3+	-	-

\*Microscopic examination per high power field.

TABLE I-D-5 (Continued)

## URINALYSIS

4-WEEKS - DIMP - FEMALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	MICROSCOPIC EXAMINATION/HPF*										CRYSTALS	
								BILI-RUBIN	OCULT BLOOD	WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	Y.P.	Ca O. OTHER	
GROUP 1 - CONTROL																			
111280	Y	Hazy	1.050	9	2+	0	0	0	0	4-8	-	0-2	-	-	3+	-	1+	-	
111281	Y	Hazy	1.032	8	2+	0	0	0	0	4-8	-	0-1	-	1+	3+	-	3+	-	
111282	Y	Hazy	1.085	6	3+	0	0	0	+	0-3	10-15	1-3	-	-	-	-	-	-	
111283	Y	Clear	1.060	5	1+	0	0	0	0	2-3	3-4	1-2	-	-	-	-	-	-	
111284	Y	Clear	1.030	5	0	0	0	0	0	2-3	-	-	-	-	3+	-	3+	-	
GROUP 2 - 300 ppm																			
111344	Y	Cloudy	1.028	6	0	0	0	0	0	0-1	-	0-1	-	-	4+	-	-	-	
111345	Y	Hazy	1.034	8	4+	0	0	0	0	0-3	-	4-8	-	-	1+	-	3+	-	
111346	Y	Clear	1.064	5	3+	0	0	0	0	6-8	4-5	+	-	-	-	-	-	-	
111347	Y	Cloudy	1.013	6	0	0	0	0	0	4-5	0-1	-	-	-	4+	-	-	-	
111348	Y	Clear	1.028	5	1+	0	0	0	0	2-3	-	2-3	-	-	-	-	-	-	
GROUP 3 - 1000 ppm																			
111408	Y	Cloudy	1.024	9	0	0	0	0	0	-	-	-	-	3+	4+	-	3+	-	
111409	Y	Hazy	1.050	7	2+	0	0	0	+	4-8	10-15	10-15	-	-	-	-	2+	-	
111410	Y	Clear	1.050	5	2+	0	0	0	0	4-5	3-4	-	-	-	-	-	-	-	
111411	Y	Clear	1.033	6	0	0	0	0	0	1-2	-	-	-	-	+	-	-	-	
111412	Y	Cloudy	1.015	7	0	0	0	0	0	2-3	-	-	-	-	3+	-	2+	-	
GROUP 4 - 3000 ppm																			
111474	Y	Hazy	1.070	8	4+	0	0	0	0	0-1	0-3	0-3	-	-	3+	-	2+	-	
111475	Y	Clear	1.042	5	1+	0	0	0	0	4-5	1-2	-	-	-	+	-	-	-	
111476	Y	Clear	1.028	6	0	0	0	0	0	2-3	-	-	-	-	3+	-	2+	-	

\*Microscopic examination per high power field.

TABLE I-D-5 (Continued)

## URINALYSIS

13-WEEKS - DIMP - FEMALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	BILI-RUBIN	OCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*										CRYSTALS																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	T.P.	Ca	O.				OTHER																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																									
GROUP 1 - CONTROL																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																
11288	Y	Hazy	1.060	5	3+	0	2+	0	0	-	0-3	-	-	2+	1+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

\*Microscopic examination per high power field.

TABLE I-D-6  
BLOOD CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>RED CELLS</u> $\mu\text{U/ml}$	<u>PLASMA</u> $\mu\text{U/ml}$
	<u>MALES</u>	
<u>1 - CONTROL</u>		
NO. SAMPLES	3	3
MEAN	207	673
S.E.	23	211
<u>2 - 300 ppm</u>		
NO. SAMPLES	4	4
MEAN	211	523
S.E.	31	39
<u>3 - 1000 ppm</u>		
NO. SAMPLES	4	4
MEAN	240	782
S.E.	35	245
<u>4 - 3000 ppm</u>		
NO. SAMPLES	4	4
MEAN	155	795
S.E.	21	198

TABLE I-D-6 (Continued)  
BLOOD CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>RED CELLS <math>\mu\text{U}/\text{ml}</math></u>	<u>PLASMA <math>\mu\text{U}/\text{ml}</math></u>
	<u>MALES</u>	
<u>1 - CONTROL</u>		
NO. SAMPLES	3	4
MEAN	189	925
S.E.	19	34
<u>2 - 300 ppm</u>		
NO. SAMPLES	4	4
MEAN	285	469
S.E.	56	31
<u>3 - 1000 ppm</u>		
NO. SAMPLES	5	5
MEAN	460	564
S.E.	19	27
<u>4 - 3000 ppm</u>		
NO. SAMPLES	4	4
MEAN	222	1229
S.E.	72	64

TABLE I-D-6 (Continued)  
BLOOD CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>RED CELLS</u> $\mu\text{U}/\text{ml}$	<u>PLASMA</u> $\mu\text{U}/\text{ml}$
	<u>FEMALES</u>	
<u>1 - CONTROL</u>		
NO. SAMPLES	4	4
MEAN	165	937
S.E.	32	207
<u>2 - 300 ppm</u>		
NO. SAMPLES	4	4
MEAN	141	1447
S.E.	34	353
<u>3 - 1000 ppm</u>		
NO. SAMPLES	4	4
MEAN	132	1466
S.E.	41	319
<u>4 - 3000 ppm</u>		
NO. SAMPLES	3	3
MEAN	169	1401
S.E.	13	137

TABLE I-D-6 (Continued)  
BLOOD CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
13 WEEKS - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>RED CELLS <math>\mu\text{U}/\text{ml}</math></u>	<u>PLASMA <math>\mu\text{U}/\text{ml}</math></u>
	<u>FEMALES</u>	
<u>1 - CONTROL</u>		
NO. SAMPLES	3	3
MEAN	143	2361
S.E.	10	29
<u>2 - 300 ppm</u>		
NO. SAMPLES	4	5
MEAN	252	2062
S.E.	86	147
<u>3 - 1000 ppm</u>		
NO. SAMPLES	4	4
MEAN	134	1977
S.E.	40	301
<u>4 - 3000 ppm</u>		
NO. SAMPLES	3	3
MEAN	114	912
S.E.	40	40

TABLE I-D-7  
BRAIN CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
MALES - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BRAIN μU/mg Tissue</u>
<u>1 - CONTROL</u>	
NO. SAMPLES	5
MEAN	14.73
S.E.	4.7
<u>2 - 300 ppm</u>	
NO. SAMPLES	5
MEAN	16.69
S.E.	6.2
<u>3 - 1000 ppm</u>	
NO. SAMPLES	5
MEAN	13.16
S.E.	4.1
<u>4 - 3000 ppm</u>	
NO. SAMPLES	5
MEAN	11.59
S.E.	2.8

TABLE I-D-7 (Continued)  
BRAIN CHOLINESTERASE ACTIVITY  
GROUP MEANS AND STANDARD ERROR  
FEMALES - DIMP

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BRAIN μU/mg Tissue</u>
<u>1 - CONTROL</u>	
NO. SAMPLES	5
MEAN	11.17
S.E.	1.4
<u>2 - 300 ppm</u>	
NO. SAMPLES	5
MEAN	7.29
S.E.	1.3
<u>3 - 1000 ppm</u>	
NO. SAMPLES	5
MEAN	7.00
S.E.	1.2
<u>4 - 3000 ppm</u>	
NO. SAMPLES	5
MEAN	9.36
S.E.	2.4

TABLE I-D-8  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 1 - CONTROL

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11244	437.4	2.0430	0.0170	1.5450	17.7050	1.0240	4.0110	0.0630	5.1250
11249	344.0	1.5370	0.0250	1.1760	13.4550	0.6790	2.4650	0.0	5.0110
11250	355.0	1.6540	0.0140	1.0510	15.1500	0.6320	3.2020	0.0540	4.7250
11251	400.0	1.4370	0.0240	1.2460	18.0020	0.6690	3.7290	0.0660	5.9110
11252	384.0	1.4770	0.0170	1.2800	13.6060	0.7470	3.0640	0.0530	5.7600
11253	296.0	1.7080	0.0210	1.1110	13.9240	0.5440	3.0460	0.0650	3.7750
11254	333.0	1.7870	0.0140	1.1610	12.4500	0.5630	2.9890	0.0620	4.7880
11255	374.0	1.7440	0.0270	1.3860	16.5350	0.6510	3.2400	0.0630	4.9010
11256	444.4	1.4310	0.0270	1.3470	18.1390	0.7660	3.7550	0.0	6.2730
11258	450.6	1.4440	0.0200	1.0430	21.9080	0.9680	4.6010	0.0660	6.0300
11259	354.4	1.4080	0.0300	1.2710	14.3740	0.6290	3.3450	0.0480	5.2440
11260	383.4	1.7960	0.0220	1.3740	14.2030	0.6370	3.5370	0.0550	5.3030
11261	373.6	1.1350	0.0360	1.1160	14.3580	0.7130	3.2630	0.0550	4.8730
11262	394.4	0.0	0.0200	1.3540	16.7880	0.6840	3.2300	0.0650	5.0260
11263	373.6	1.6520	0.0250	1.3420	14.1570	0.7110	3.0350	0.0	5.1680
11264	349.0	1.7460	0.0350	1.3890	14.9330	0.8540	3.3540	0.0560	5.0060
11265	397.4	1.5450	0.0240	1.4640	16.5170	0.7450	3.5780	0.0550	5.2460
11266	434.0	1.7380	0.0230	1.2340	21.2980	0.7940	3.5580	0.0410	5.3840
11267	340.4	1.7880	0.0	1.5370	18.4120	0.7210	3.5570	0.0530	5.1600
11268	375.0	1.7550	0.0160	1.4260	15.6020	0.7470	3.3400	0.0490	5.0590
11269	360.0	1.4940	0.0300	1.4450	15.4890	1.0200	3.5500	0.0500	5.3440
11270	440.3	1.8220	0.0260	1.3740	15.5750	0.7540	3.6750	0.0490	5.9250
11271	345.0	1.6580	0.0	2.0550	14.4600	0.4260	3.5740	0.0	5.1910
11272	381.0	1.7440	0.0240	1.4010	14.1120	0.7410	3.1740	0.0490	3.2170
11274	388.5	1.7220	0.0140	1.3000	15.8300	0.6560	3.1700	0.0510	5.3700
11275	424.0	1.8160	0.0190	1.5770	18.2390	0.7140	3.5200	0.0560	5.3800
11276	413.1	1.6430	0.0320	1.3640	14.9850	0.7030	3.7690	0.0650	5.4420
11277	256.6	1.7240	0.0190	1.3230	10.0720	0.6050	2.7920	0.0600	1.8540
11278	436.4	1.7860	0.0220	1.4140	14.9250	0.8310	3.6770	0.0540	5.3340
11279	444.3	1.7430	0.0270	1.5410	17.8900	0.7230	3.8290	0.0550	5.2340
N	30	24	24	30	30	30	30	26	30
MEAN	387.5	1.7268	0.0234	1.3589	16.1498	0.7387	3.4358	0.0561	5.0703
S.D.	44.4	0.1621	0.0058	0.1476	2.6527	0.1207	0.3745	0.0067	0.8464
S.E.	8.1	0.0331	0.0011	0.0361	0.4456	0.0220	0.0684	0.0013	0.1545

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 2 - 300 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	SKIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11312	402.4	1.8340	0.0120	1.6020	14.5510	0.6550	3.3130	0.0530	5.1650
11313	296.0	1.6340	0.0300	1.2680	12.7400	0.5720	3.1960	0.0620	0.0
11314	381.6	1.8680	0.0450	1.3480	17.9490	0.5970	3.7090	0.0700	5.3390
11315	403.5	1.6910	0.0300	1.2890	15.5740	0.6440	3.4270	0.0610	5.6310
11316	351.0	1.8100	0.0190	1.3860	17.4100	0.5630	3.3920	0.0690	5.0780
11317	259.0	1.6600	0.0220	0.9100	10.1820	0.5110	2.4840	0.0490	3.1550
11318	314.0	1.7620	0.0250	1.3190	12.4140	0.6670	2.5920	0.0580	3.7090
11319	342.0	1.7100	0.0200	1.0470	12.2720	0.6570	3.0590	0.0610	5.5050
11320	345.6	1.8370	0.0290	1.4430	15.8610	0.8230	3.8360	0.0560	5.6540
11321	410.5	1.8830	0.0200	1.3040	19.4970	0.8140	3.9630	0.0670	5.1810
11322	349.4	1.6540	0.0220	1.4100	17.9440	0.7630	3.6600	0.0400	4.7780
11323	385.4	1.6250	0.0230	1.4140	15.5510	0.7220	3.8370	0.0600	5.6220
11325	402.0	1.8080	0.0250	1.3660	15.4300	0.6470	3.8580	0.0480	5.2240
11326	431.0	1.8250	0.0230	1.3930	17.0000	0.6590	3.8220	0.0650	5.1760
11327	376.4	1.4200	0.0250	1.2600	14.4840	0.7020	3.5700	0.0540	5.1240
11328	477.0	1.7240	0.0250	1.9250	20.3420	0.7820	3.9390	0.0610	5.4380
11329	413.0	1.7700	0.0100	1.4120	19.0680	0.6590	3.9340	0.0540	4.9670
11330	384.0	0.0	0.0240	0.0	0.0	0.0	0.0	0.0540	0.0
11331	426.0	1.7490	0.0210	1.4600	2.2480	0.7770	4.4290	0.0670	5.4510
11332	422.8	1.7770	0.0190	1.6030	17.8790	0.8500	3.8650	0.0630	5.4590
11333	424.0	1.6970	0.0270	1.6700	19.5040	0.8180	3.4340	0.0700	5.3880
11334	417.0	1.7300	0.0240	1.2460	16.5910	0.7730	3.6770	0.0720	5.2430
11335	415.1	1.7130	0.0290	1.4870	17.2750	0.6910	3.9330	0.0590	4.8970
11336	251.8	1.6840	0.0250	1.0150	10.1240	0.5710	2.7410	0.0	2.7730
11337	420.0	1.5190	0.0230	1.2750	17.6850	0.6490	4.3890	0.0650	5.2890
11338	420.8	1.4490	0.0190	1.7010	21.4960	0.7910	4.2760	0.0490	4.5670
11339	375.0	1.5400	0.0170	1.5220	13.6360	0.6840	3.2730	0.0620	4.9370
11340	341.0	1.3680	0.0250	1.2020	17.1070	0.0	3.4580	0.0580	5.3640
11341	387.0	1.7330	0.0270	1.2100	15.7180	0.6580	3.4330	0.0570	4.8570
11342	352.5	1.8400	0.0230	1.6060	12.3370	0.8430	3.1410	0.0	5.1270
11343	403.1	1.7170	0.0220	1.6190	16.7140	0.7200	3.9290	0.0670	5.3260
MEAN	31	30	31	30	30	29	30	29	29
S.D.	384.9	1.7179	0.0234	1.3904	15.5523	0.7063	3.5856	0.0597	5.0146
S.E.	44.2	0.1255	0.0062	0.2145	3.7907	0.1028	0.4793	0.0076	0.6865
	8.8	0.0229	0.0011	0.0392	0.6921	0.0191	0.0875	0.0014	0.1275

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 3 - 1000 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11376	344.0	1.9050	0.0260	1.2330	14.8010	0.5740	3.1840	0.0580	4.9920
11377	437.0	1.7520	0.0310	1.5430	15.9420	0.8400	3.9670	0.0540	5.0190
11378	429.0	1.8790	0.0290	1.3780	17.4490	0.6490	3.6750	0.0620	6.1310
11379	438.3	1.6700	0.0220	1.3890	18.8820	0.7560	3.9880	0.0710	6.1880
11380	396.0	1.7350	0.0270	1.4640	17.6750	0.6020	3.5400	0.0620	4.9200
11381	391.4	1.5130	0.0230	1.7340	17.6900	0.8410	3.8250	0.0650	5.7910
11382	350.1	1.8390	0.0190	1.2320	15.6130	0.8580	3.4650	0.0550	5.1290
11383	347.0	1.8150	0.0290	1.6540	16.1370	0.9770	4.0210	0.0560	5.4080
11384	351.0	1.6160	0.0270	1.4850	17.0600	0.6480	3.8360	0.0600	5.2080
11385	431.1	1.8480	0.0230	1.6940	17.5430	0.8770	3.9140	0.0540	5.8620
11386	214.1	1.6590	0.0200	0.8770	7.8770	0.4580	1.9040	0.0700	0.0880
11387	321.4	1.6280	0.0240	0.9870	15.2100	0.3030	2.9430	0.0550	4.9920
11388	347.0	1.8490	0.0090	1.4650	15.0070	0.7150	3.6330	0.0430	5.1680
11389	397.1	1.9620	0.0290	1.4380	17.6800	0.6170	3.7300	0.0580	5.6090
11390	373.2	1.8390	0.0	1.4930	15.3670	0.5290	3.3400	0.0550	4.4930
11391	392.5	1.8720	0.0230	1.6520	20.3800	0.7330	4.1600	0.0560	5.4030
11392	434.4	1.9910	0.0320	1.6900	21.2850	0.8810	3.9680	0.0	5.1720
11393	342.1	1.8110	0.0270	1.2260	18.6940	0.6740	3.5310	0.0	4.9230
11394	384.6	1.7910	0.0190	1.3040	15.9400	0.6260	3.4800	0.0570	4.9850
11395	409.4	1.7760	0.0260	1.6020	14.6670	0.6860	3.4920	0.0610	5.3790
11396	392.0	1.6160	0.0260	1.2210	16.6300	0.6720	3.2240	0.0610	4.9210
11397	344.0	1.7360	0.0220	1.1760	13.9210	0.8700	2.8890	0.0650	4.3240
11398	415.0	1.7000	0.0300	1.4420	19.0050	0.7430	4.4220	0.0660	5.9830
11399	407.0	1.5450	0.0190	1.5830	16.7000	0.7540	3.1820	0.0500	5.0690
11400	377.2	1.7400	0.0170	1.3260	15.2960	0.6420	3.4350	0.0530	5.4710
11401	300.3	1.8640	0.0210	1.2220	12.1330	0.4720	2.6600	0.0520	4.9250
11402	403.3	1.8210	0.0220	1.3640	16.3460	0.7230	3.8520	0.0560	5.1410
11403	381.0	1.9140	0.0180	1.4500	15.3050	0.6900	3.3400	0.0500	5.4850
11404	361.0	1.7810	0.0150	1.1890	15.1660	0.5950	3.5960	0.0480	5.0410
11405	402.8	1.9190	0.0220	1.4770	16.6270	0.7670	3.3540	0.0530	5.1710
11406	427.4	1.8550	0.0210	1.6060	16.9870	0.7400	3.7440	0.0570	5.1860
11407	360.0	1.7440	0.0200	1.1630	12.8340	0.6440	3.4000	0.0430	4.8410
N	32	32	31	32	32	32	32	30	32
46.47	374.7	1.7810	0.0232	1.3987	16.1843	0.6952	3.5217	0.0569	5.0756
5.0.	45.7	0.1175	0.0050	0.2083	2.4730	0.1406	0.4821	0.0068	1.0039
5.4.	4.1	0.0208	0.0004	0.0368	0.4372	0.0249	0.0852	0.0012	0.1775

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 4 - 3000 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11440	383.0	1.8370	0.0230	1.3850	13.2170	0.5880	3.1150	0.0540	5.1680
11441	379.0	1.7650	0.0240	1.3600	15.2760	0.6660	3.6290	0.0600	5.2380
11442	425.0	1.8060	0.0260	1.8420	20.9520	0.7240	3.7580	0.0570	5.2830
11443	402.0	1.7430	0.0270	1.2820	15.2170	0.7200	3.6360	0.0700	5.5850
11444	379.0	1.7480	0.0	1.4540	15.8110	0.8720	3.6230	0.0730	5.1200
11445	372.2	1.7410	0.0260	1.4600	13.2300	0.5420	3.3330	0.0520	4.6380
11446	232.4	1.7400	0.0260	1.4000	15.8730	0.8120	3.6660	0.0560	4.8970
11447	204.4	1.4650	0.0270	1.2500	9.4400	0.4340	2.5400	0.0740	1.7640
11448	202.0	1.8490	0.0270	0.8080	8.2050	0.4130	2.0810	0.0600	1.0640
11449	453.0	1.8590	0.0250	1.5090	18.8510	0.8570	4.2800	0.0620	6.2780
11450	360.6	1.8260	0.0240	1.3070	15.5810	0.6490	3.5250	0.0670	5.2640
11451	419.0	1.8720	0.0310	1.8990	21.1970	0.9500	4.3890	0.0600	5.7110
11454	352.0	1.7470	0.0200	1.1430	15.6450	0.7000	3.0460	0.0720	4.8800
11453	386.0	1.7630	0.0250	1.3490	19.1200	0.6710	3.7570	0.0520	5.0120
11455	378.0	2.0830	0.0250	1.7100	16.3100	1.0290	3.9860	0.0630	5.2870
11456	394.5	2.1490	0.0290	1.6360	17.5020	1.1160	4.1490	0.0570	5.6680
11457	336.5	1.7900	0.0310	1.4620	15.0440	0.6930	3.5200	0.0	5.6850
11459	378.3	1.9080	0.0250	1.5710	14.3990	0.8220	3.2580	0.0660	5.5090
11460	405.0	1.8180	0.0240	1.3810	20.0840	0.7400	3.5660	0.0680	5.1010
11461	335.5	1.8250	0.0240	1.2610	20.2880	1.0080	4.1690	0.0840	5.3310
11462	340.4	1.7660	0.0290	1.3650	17.7800	0.6550	3.2140	0.0550	4.8740
11463	408.0	1.6100	0.0150	1.5180	15.8670	0.7720	3.3320	0.0620	5.2120
11464	414.0	1.7810	0.0240	1.6100	17.9140	0.7600	4.0760	0.0540	5.4750
11465	342.4	1.4460	0.0150	1.2720	15.1790	0.7290	3.0760	0.0330	5.5120
11466	415.0	1.7860	0.0210	1.3630	17.6670	0.8040	3.6150	0.0500	5.3450
11467	363.2	1.8450	0.0210	1.3930	19.8690	0.7910	4.0350	0.0530	5.2860
11468	381.4	1.8400	0.0240	1.2960	18.6400	0.7060	3.9110	0.0590	4.9990
11469	402.0	1.9270	0.0140	1.5120	15.2370	0.6150	3.7240	0.0490	4.7390
11470	327.0	1.4030	0.0330	1.1430	13.9260	0.6640	3.1060	0.0500	4.4910
N	29	29	24	29	29	29	29	28	29
MEAN	366.9	1.7889	0.0245	1.4187	16.3216	0.7431	3.5557	0.0597	4.9799
S.D.	60.1	0.1565	0.0045	0.2134	3.0772	0.1569	0.5106	0.0100	1.0571
S.E.	11.2	0.0291	0.0009	0.0396	0.5714	0.0291	0.0948	0.0019	0.1963

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 1 - CONTROL

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11280	245.0	1.6180	0.0230	0.8550	9.2200	0.5420	2.1170	0.0830	0.1280
11281	224.0	1.4890	0.0240	1.0320	9.9040	0.6440	2.1360	0.0	0.3120
11282	247.0	1.7080	0.0270	0.0	9.9980	0.5790	2.3440	0.1030	0.1480
11283	248.4	1.8400	0.0240	1.0860	10.0030	0.4650	2.3930	0.0840	0.1040
11284	235.6	1.6240	0.0240	1.0770	7.8920	0.5850	1.9370	0.0750	0.1300
11285	273.4	1.4910	0.0200	1.1680	9.9860	0.4410	2.2420	0.0950	0.1460
11286	250.0	1.7870	0.0170	0.9810	8.4210	0.5190	2.1370	0.0	0.1220
11287	242.0	1.5840	0.0170	0.9240	9.0730	0.5140	1.9650	0.0790	0.1440
11288	244.8	1.8300	0.0160	0.8790	8.7810	0.5080	2.0300	0.0690	0.0970
11289	235.2	1.5080	0.0210	1.0100	8.7990	0.5580	2.2300	0.0	0.1290
11290	239.2	1.6560	0.0180	0.8420	11.3520	0.5420	2.3550	0.0860	0.1410
11291	226.1	1.6570	0.0310	1.1430	10.4930	0.5630	2.0220	0.0880	0.1090
11292	215.0	1.5550	0.0250	0.8770	9.3020	0.4590	2.0450	0.0840	0.1490
11293	235.0	1.4350	0.0190	1.1630	11.2720	0.6460	2.0360	0.0790	0.1180
11294	251.1	1.6800	0.0220	1.1490	10.3940	0.4870	2.1540	0.0980	0.1340
11295	232.4	1.5310	0.0210	1.0060	10.9260	0.4790	2.1480	0.0940	0.0920
11296	255.4	1.6810	0.0200	1.1940	9.9700	0.5440	2.2080	0.0800	0.1480
11297	238.0	1.6280	0.0160	0.8960	7.5770	0.4820	1.9870	0.0800	0.1310
11298	253.0	1.2940	0.0300	1.2730	9.2070	0.5420	1.9070	0.0700	0.1440
11299	229.0	0.0	0.0180	0.7400	7.2950	0.5620	1.8180	0.0810	0.1390
11300	241.0	1.4570	0.0140	0.9000	9.4230	0.4190	2.2900	0.0990	0.0870
11301	224.0	1.5580	0.0220	1.0560	8.9840	0.4720	2.0790	0.0840	0.1070
11302	254.1	1.7370	0.0280	0.9350	9.9320	0.6720	2.3040	0.0930	0.1480
11303	232.0	1.4720	0.0220	0.9360	8.0680	0.4970	1.9640	0.0710	0.1550
11304	217.8	1.6920	0.0240	0.8630	9.3970	0.4760	2.2190	0.0810	0.0140
11305	239.0	1.5780	0.0230	0.9520	8.3860	0.4990	2.0420	0.0670	0.1670
11306	227.0	1.5320	0.0250	0.9350	8.3250	0.4730	2.0690	0.0950	0.1490
11307	223.8	1.6570	0.0210	1.0360	9.4250	0.4720	2.1790	0.0750	0.1230
11308	236.7	1.5360	0.0210	0.8750	10.0450	0.5370	2.2560	0.0700	0.0650
11309	245.0	1.5290	0.0320	0.9610	10.8510	0.5590	2.1540	0.0750	0.1610
11310	247.0	1.6350	0.0220	0.7970	9.5680	0.4490	2.3180	0.0860	0.1480
11311	258.0	1.6570	0.0230	1.0600	11.0060	0.6150	2.3120	0.1060	0.1330
4	32	31	32	31	32	32	32	29	32
4880	240.0	1.5005	0.0225	0.9918	9.4461	0.5206	2.1390	0.0838	0.1319
500	12.7	0.1188	0.0045	0.1309	1.0579	0.0635	0.1459	0.0106	0.0450
505	2.2	0.0213	0.0008	0.0235	0.1870	0.0112	0.0258	0.0020	0.0080

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 2 - 300 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11344	238.3	1.7000	0.0210	0.9250	0.0	0.5080	2.0810	0.0690	0.0850
11345	271.0	1.6260	0.0210	0.9950	9.4360	0.5290	2.2510	0.0770	0.1390
11346	230.5	1.8550	0.0310	0.9980	7.6910	0.5780	1.8700	0.0620	0.1060
11347	240.3	1.6670	0.0220	1.0000	8.3580	0.5020	2.2410	0.0660	0.1150
11348	228.0	1.6080	0.0230	0.8770	9.0490	0.4910	2.0580	0.0770	0.0960
11349	221.9	1.7260	0.0150	0.8110	7.2060	0.4730	1.9820	0.0730	0.0820
11350	254.4	1.6750	0.0240	0.9350	8.9270	0.5470	2.0140	0.0700	0.1080
11351	254.2	1.6740	0.0230	1.0350	11.2360	0.5220	2.3600	0.0820	0.1150
11352	225.0	1.5840	0.0220	0.8840	8.6080	0.5180	2.1620	0.0790	0.0920
11353	235.1	1.5160	0.0240	0.9310	8.6480	0.5230	2.1330	0.0650	0.1130
11354	224.0	1.5780	0.0230	0.7450	7.6780	0.3980	2.1290	0.0660	0.1050
11355	233.0	1.6920	0.0190	0.8940	9.7700	0.5400	2.2550	0.0940	0.1230
11356	223.0	1.5900	0.0240	0.8520	9.2240	0.5480	2.2710	0.0700	0.1370
11357	268.0	1.8910	0.0230	1.3150	9.6730	0.6110	2.4120	0.0830	0.1580
11358	244.8	1.5220	0.0210	0.9280	10.3690	0.5590	2.1530	0.0670	0.0830
11359	233.1	1.5290	0.0210	0.8490	0.0	0.5530	2.1850	0.0730	0.3290
11360	234.0	1.5960	0.0240	0.9710	9.5920	0.5590	2.1310	0.0790	0.1220
11361	210.0	1.6770	0.0230	0.6850	7.2350	0.4620	1.7380	0.0660	0.0870
11362	239.0	1.5900	0.0180	1.2700	8.2000	0.5400	1.8670	0.0740	0.1430
11363	246.6	1.7850	0.0200	1.0250	9.9470	0.6170	2.4540	0.0820	0.1090
11364	158.9	1.6050	0.0310	0.8540	8.2110	0.4240	1.9240	0.0650	0.1760
11365	211.0	1.6140	0.0170	0.9310	5.8880	0.4100	1.7750	0.0630	0.0670
11366	239.0	1.5440	0.0130	0.8640	7.6100	0.6100	1.8970	0.0550	0.0890
11367	233.0	1.5150	0.0220	1.0460	7.8230	0.5030	2.0300	0.0710	0.1090
11368	256.2	1.8980	0.0240	1.0360	11.8850	0.5710	2.2950	0.0950	0.1270
11369	224.2	1.2900	0.0210	0.9130	7.4880	0.3850	1.8100	0.0820	0.1040
11370	232.5	1.7700	0.0210	0.9200	8.7680	0.5360	2.0020	0.0880	0.1330
11371	273.4	1.7390	0.0250	1.2850	10.1470	0.6330	2.2020	0.0760	0.1350
11471	361.3	1.7180	0.0240	1.1790	18.3180	0.6480	3.5450	0.0510	4.8150
11372	238.0	1.7080	0.0190	1.0900	9.8500	0.5080	2.2100	0.0840	0.1420
11373	237.0	1.6500	0.0230	1.0890	9.7920	0.6060	2.0070	0.0950	0.1660
11474	276.0	1.6910	0.0230	1.0800	10.1450	0.6120	2.2490	0.0900	0.1830
11375	249.0	1.7470	0.0270	1.2860	9.4950	0.5500	2.0750	0.0910	0.1480
N	33	33	43	33	31	33	33	33	33
M.F.	240.7	1.6355	0.0224	0.9849	9.2344	0.5325	2.1460	0.0752	0.2679
S.O.	30.5	0.1080	0.0034	0.1531	2.1148	0.0664	0.3097	0.0113	0.8176
S.F.	5.3	0.0188	0.0007	0.0267	0.3798	0.0116	0.0539	0.0020	0.1423

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 3 - 1000 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11408	283.0	1.5180	0.0230	1.0860	10.2140	0.6750	2.3090	0.0840	0.1430
11409	245.1	1.6080	0.0170	1.0440	8.2900	0.4440	2.0330	0.0610	0.1140
11410	249.0	1.7030	0.0250	0.8830	8.0500	0.5150	2.0910	0.0630	0.0670
11411	222.0	1.6810	0.0160	0.8900	8.0900	0.4400	1.9070	0.0860	0.1080
11412	251.0	1.6740	0.0270	0.9600	11.2290	0.5470	2.2100	0.0	0.1480
11413	256.0	1.6590	0.0210	0.9300	8.7540	0.5490	2.2990	0.0860	0.1450
11414	230.0	1.5730	0.0170	1.0650	8.7970	0.4260	2.2780	0.0800	0.1370
11415	218.0	1.5780	0.0210	0.8820	7.6290	0.5510	2.0980	0.0760	0.0950
11416	244.8	1.6700	0.0260	1.0020	9.2870	0.5500	2.4020	0.1000	0.1220
11417	223.4	1.5550	0.0150	0.9380	9.6210	0.5360	2.2770	0.0720	0.1120
11418	265.0	1.5410	0.0210	1.0120	9.7170	0.5340	2.4020	0.0920	0.1000
11419	229.0	1.7190	0.0140	1.1340	7.7360	0.4720	2.0440	0.0760	0.1080
11420	256.1	1.7070	0.0140	1.1360	9.3490	0.5400	2.2760	0.0800	0.1680
11421	225.3	1.6580	0.0230	0.8990	7.0240	0.5470	1.9780	0.0	0.1160
11422	217.2	1.6820	0.0	0.9700	8.1180	0.5270	2.0410	0.0830	0.1920
11423	245.4	1.4530	0.0260	0.9210	8.5150	0.5480	2.3220	0.0670	0.1350
11424	232.0	1.5860	0.0210	1.0190	9.3450	0.5520	2.1060	0.0790	0.1250
11425	268.0	1.7290	0.0180	1.0630	11.8630	0.6090	2.5930	0.0920	0.1590
11426	261.4	1.6680	0.0170	0.8530	9.9680	0.5330	2.0930	0.0730	0.0740
11427	247.0	1.2910	0.0220	0.9550	9.0690	0.4820	1.9760	0.0710	0.1230
11428	262.0	1.6290	0.0160	1.0730	10.9210	0.5770	2.2610	0.0890	0.1980
11429	262.6	1.7620	0.0180	0.9440	10.4180	0.6350	2.4300	0.0990	0.1410
11430	232.0	1.5290	0.0200	1.0110	10.0090	0.5560	2.1000	0.1010	0.1670
11431	240.0	1.5230	0.0280	1.1980	8.7190	0.5120	2.0840	0.0770	0.1370
11432	243.0	1.6370	0.0200	0.8550	9.3670	0.5100	2.2780	0.0700	0.2050
11433	242.1	1.6570	0.0230	0.9660	10.3850	0.5030	2.2020	0.0760	0.0930
11434	218.0	1.5890	0.0190	0.7890	8.7400	0.5840	2.0210	0.0780	0.1420
11435	246.4	1.6740	0.0170	0.8710	10.9160	0.7230	2.1470	0.0720	0.0760
11436	252.4	1.6540	0.0240	0.9670	10.1900	0.6020	2.1820	0.0860	0.1590
11437	258.0	1.6010	0.0130	0.9580	9.0470	0.4790	2.0360	0.0800	0.0980
11438	224.6	1.5670	0.0220	0.9830	9.2620	0.5100	2.0500	0.0950	0.1250
11439	253.2	1.7610	0.0300	0.9770	10.4700	0.5680	2.3400	0.0950	0.1130
N	32	32	31	32	32	32	32	30	32
48.87	244.2	1.6467	0.0204	0.9761	9.3471	0.5424	2.1833	0.0813	0.1295
S.E.	18.6	0.1068	0.0041	0.0919	1.1347	0.0631	0.1583	0.0107	0.0343
S.E.	2.4	0.0189	0.0007	0.0163	0.2006	0.0111	0.0280	0.0020	0.0061

TABLE I-D-8 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 4 - 3000 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	SKIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11472	257.6	1.6540	0.0160	0.8660	8.8060	0.5230	2.0090	0.0600	0.1370
11473	244.0	1.6630	0.0190	0.8740	9.4050	0.5360	2.1950	0.0	0.1190
11474	234.4	1.7050	0.0230	0.8080	8.7430	0.4390	2.2290	0.0800	0.0780
11475	241.2	1.1440	0.0200	1.0210	8.8820	0.5190	2.2570	0.0840	0.1350
11476	221.1	1.5540	0.0220	0.9250	9.3470	0.5340	2.2420	0.0660	0.1480
11477	206.4	1.6480	0.0240	0.9100	8.9700	0.4300	2.0130	0.0690	0.1160
11478	209.7	1.5170	0.0180	0.9730	9.0810	0.5020	2.1320	0.0590	0.1030
11479	244.6	1.7660	0.0200	0.9100	8.8600	0.5620	2.1630	0.0900	0.1290
11480	250.0	1.6850	0.0190	1.0520	10.0560	0.5390	2.1590	0.0690	0.1380
11481	226.3	1.4500	0.0250	1.0680	8.6300	0.5440	2.1590	0.0750	0.1080
11482	224.0	1.6970	0.0230	0.8550	7.9520	0.4270	1.8480	0.0630	0.1240
11483	247.0	1.4220	0.0190	1.0830	9.9300	0.5310	2.1260	0.0660	0.1470
11484	247.0	1.6220	0.0230	0.8420	9.2270	0.6170	2.1630	0.0550	0.0830
11485	352.0	1.8090	0.0220	1.7810	14.9600	0.6600	3.5390	0.0460	4.6850
11486	225.8	1.5370	0.0160	1.0190	8.0930	0.4650	2.1510	0.0640	0.0930
11487	230.4	1.5460	0.0170	0.9240	8.4260	0.4610	2.0460	0.0710	0.1270
11488	148.5	1.3890	0.0190	0.8520	7.2200	0.3860	1.4510	0.0430	0.1100
11489	241.8	1.7340	0.0300	1.0440	9.7120	0.6170	1.8670	0.0570	0.1240
11490	220.6	1.6270	0.0220	0.9230	7.8630	0.5640	1.8540	0.0640	0.1050
11491	197.0	1.4300	0.0210	0.6880	7.8810	0.5460	1.8880	0.0460	0.0910
11492	259.0	1.7080	0.0160	0.9580	10.2260	0.6210	2.1420	0.0820	0.1520
11493	216.0	1.6470	0.0200	0.8210	7.7500	0.4540	2.0600	0.0700	0.0650
11494	240.0	1.5810	0.0320	0.8420	8.4900	0.5100	1.8850	0.0550	0.1330
11495	236.4	1.7740	0.0230	0.8840	9.0740	0.4610	2.1840	0.0670	0.1080
11496	272.4	1.7500	0.0240	1.0340	10.1000	0.4810	2.2480	0.0770	0.1430
11497	249.5	1.3670	0.0300	0.9760	10.9470	0.5850	2.4030	0.0680	0.0940
11498	257.0	1.5930	0.0230	1.3310	10.4170	0.5520	1.9610	0.0680	0.2370
11499	280.2	1.5420	0.0240	1.1810	12.3280	0.6780	2.4380	0.0830	0.1280
11500	246.0	1.6670	0.0140	0.8750	11.2370	0.5560	2.3000	0.0760	0.0810
11501	230.3	1.4700	0.0	1.1340	11.2650	0.4540	2.0910	0.0810	0.1040
11502	371.4	1.8820	0.0270	1.7730	20.2890	0.6410	3.4040	0.0570	5.2010
11503	228.0	1.7890	0.0230	1.3460	10.9140	0.4970	2.1230	0.0	0.1540
N	32	32	31	32	32	32	32	30	32
MEAN	242.7	1.5406	0.0214	1.0174	9.8309	0.5279	2.1791	0.0670	0.4220
S.D.	34.4	0.1609	0.0041	0.2446	2.4525	0.0721	0.3881	0.0118	1.1842
S.E.	7.0	0.0284	0.0007	0.0432	0.4335	0.0127	0.0686	0.0022	0.2100

TABLE I-D-9  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 1 - CONTROL

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11248	0.4671	0.0039	0.3647	4.0478	0.2341	0.9170	0.0144	1.1717
11249	0.4488	0.0073	0.3419	4.0276	0.1974	0.8328	0.0	1.4567
11250	0.4654	0.0039	0.2961	4.2676	0.1780	0.9020	0.0152	1.3310
11251	0.3543	0.0060	0.3115	4.5005	0.1672	0.4322	0.0165	1.4777
11252	0.4448	0.0044	0.3333	3.5432	0.1945	0.7992	0.0138	1.5000
11253	0.5170	0.0071	0.3753	4.7041	0.1851	1.0291	0.0220	1.2753
11254	0.5346	0.0057	0.3486	3.7387	0.1691	0.8976	0.0186	1.4378
11255	0.4676	0.0072	0.3706	4.4211	0.1741	0.8663	0.0168	1.3104
11256	0.4074	0.0060	0.2997	4.0363	0.1704	0.8356	0.0	1.3959
11258	0.4042	0.0044	0.2315	4.8620	0.2148	1.0211	0.0146	1.3382
11259	0.5045	0.0084	0.3546	4.0106	0.1755	0.9445	0.0134	1.4632
11260	0.4584	0.0057	0.3584	3.7045	0.1661	0.9225	0.0143	1.3832
11261	0.3038	0.0096	0.2487	3.8431	0.1908	0.8734	0.0147	1.3043
11262	0.0	0.0051	0.3441	4.2512	0.1745	0.8179	0.0165	1.2727
11263	0.4422	0.0067	0.3592	3.7493	0.1903	0.8124	0.0	1.3833
11264	0.4376	0.0088	0.3431	3.7426	0.2140	0.8406	0.0140	1.2546
11265	0.3988	0.0060	0.3597	4.1563	0.1875	0.9004	0.0138	1.3327
11266	0.4005	0.0053	0.2843	4.9074	0.1829	0.8198	0.0094	1.2406
11267	0.4644	0.0	0.4035	4.9651	0.1893	0.9338	0.0139	1.3547
11268	0.4631	0.0042	0.3763	4.1166	0.1971	0.8813	0.0129	1.3348
11269	0.5275	0.0083	0.4153	4.3025	0.2833	0.9861	0.0139	1.4844
11270	0.4134	0.0059	0.3121	3.5374	0.1712	0.8347	0.0111	1.3457
11271	0.4306	0.0	0.5340	5.1844	0.2405	0.9283	0.0	1.3483
11272	0.4577	0.0063	0.3577	3.7039	0.1945	0.8331	0.0129	0.8444
11274	0.4432	0.0036	0.3346	4.0746	0.1689	0.8160	0.0131	1.3822
11275	0.4283	0.0045	0.3719	4.3017	0.1684	0.8302	0.0132	1.2689
11276	0.3977	0.0077	0.3314	4.8378	0.1702	0.9124	0.0157	1.3174
11277	0.6719	0.0074	0.5156	3.4252	0.2358	1.0881	0.0234	0.7225
11278	0.4150	0.0051	0.3247	3.4677	0.1931	0.8543	0.0125	1.2393
11279	0.3941	0.0060	0.3430	3.9817	0.1609	0.8522	0.0122	1.1649
N	29	28	30	30	30	30	26	30
MEAN	0.4517	0.0061	0.3542	4.1551	0.1913	0.8905	0.0147	1.3046
S.D.	0.0887	0.0016	0.0543	0.4610	0.0275	0.0714	0.0030	0.1666
S.E.	0.0128	0.0003	0.0108	0.0842	0.0050	0.0130	0.0006	0.0304

TABLE I-D-9 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 2 - 300 ppm

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11312	0.4570	0.0030	0.3981	3.6161	0.1628	0.8233	0.0132	1.2835
11313	0.5520	0.0101	0.4284	4.3041	0.1432	1.0797	0.0209	0.0
11314	0.4495	0.0118	0.3532	4.7036	0.1564	0.9720	0.0183	1.3991
11315	0.4131	0.0074	0.3195	3.8597	0.1596	0.8493	0.0151	1.3955
11316	0.5157	0.0054	0.3449	4.9601	0.1604	0.9664	0.0197	1.4467
11317	0.6409	0.0085	0.3514	3.9313	0.1973	0.9591	0.0189	1.2181
11318	0.5524	0.0078	0.4135	3.8915	0.2091	0.8125	0.0182	1.1627
11319	0.5000	0.0058	0.3061	3.5883	0.1921	0.8944	0.0178	1.6096
11320	0.4644	0.0073	0.3648	4.0094	0.2080	0.9697	0.0142	1.4292
11321	0.4587	0.0049	0.3177	4.7496	0.1983	0.9654	0.0163	1.2621
11323	0.4243	0.0056	0.3617	4.6034	0.2470	0.9389	0.0103	1.2258
11324	0.4216	0.0060	0.3669	4.0350	0.1873	0.9956	0.0156	1.4587
11325	0.4498	0.0062	0.3398	3.8383	0.1609	0.9597	0.0119	1.2995
11326	0.4234	0.0053	0.3232	3.9443	0.1529	0.8868	0.0151	1.2009
11327	0.3773	0.0066	0.3348	3.8480	0.1865	0.9485	0.0143	1.3613
11328	0.3614	0.0052	0.4036	4.2646	0.1639	0.8258	0.0128	1.1400
11329	0.4286	0.0024	0.3419	4.6169	0.1596	0.9525	0.0131	1.2027
11330	0.0	0.0072	0.0	0.0	0.0	0.0	0.0139	0.0
11331	0.4106	0.0049	0.3427	0.5277	0.1824	1.0397	0.0157	1.2796
11332	0.4203	0.0045	0.3791	4.2287	0.2010	0.9141	0.0149	1.2912
11333	0.4002	0.0064	0.3439	4.6000	0.1929	0.8099	0.0165	1.2708
11334	0.4143	0.0067	0.2488	3.9787	0.1854	0.8818	0.0173	1.2573
11335	0.4127	0.0070	0.3582	4.1616	0.1665	0.9475	0.0142	1.1797
11336	0.6688	0.0099	0.4031	4.0207	0.2268	1.0886	0.0	1.1013
11337	0.3617	0.0055	0.3036	4.2107	0.1593	1.0450	0.0155	1.2593
11338	0.4513	0.0045	0.4042	5.1044	0.1880	1.0162	0.0116	1.0853
11339	0.4240	0.0045	0.4059	3.6353	0.1824	0.8728	0.0165	1.3165
11340	0.3492	0.0064	0.3074	4.3752	0.0	0.8844	0.0148	1.3719
11341	0.4478	0.0070	0.3127	4.0615	0.1700	0.8871	0.0147	1.2550
11342	0.5218	0.0065	0.4555	3.4984	0.2391	0.8908	0.0	1.4541
11343	0.4259	0.0055	0.4016	4.1464	0.1746	0.9747	0.0166	1.3213
N	30	31	30	30	29	30	29	29
MEAN	0.4544	0.0063	0.3524	4.0440	0.1851	0.9351	0.0154	1.2944
S.D.	0.0747	0.0020	0.0422	0.7780	0.0246	0.0757	0.0025	0.1188
S.E.	0.0146	0.0004	0.0077	0.1420	0.0046	0.0138	0.0005	0.0221

TABLE I-D-9 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 3 - 1000 ppm

DIMP

ANIMAL NUMBER	HEAD	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11376	0.4361	0.0068	0.3211	3.8544	0.1495	0.8292	0.0151	1.3000
11377	0.4009	0.0071	0.3531	3.6481	0.1922	0.9078	0.0124	1.1485
11378	0.4340	0.0068	0.3212	4.0790	0.1606	0.8566	0.0145	1.4291
11379	0.3810	0.0050	0.3169	4.3080	0.1725	0.9099	0.0162	1.4118
11380	0.4381	0.0068	0.3697	4.4634	0.1520	0.8939	0.0157	1.2424
11381	0.3866	0.0059	0.4430	4.5197	0.2149	0.9773	0.0166	1.4796
11382	0.5253	0.0054	0.3519	4.4596	0.2451	0.9897	0.0157	1.4650
11383	0.5231	0.0084	0.4767	4.6504	0.2816	1.1588	0.0161	1.5585
11384	0.4604	0.0077	0.4231	4.8604	0.1846	1.0929	0.0171	1.4838
11385	0.4287	0.0053	0.3429	4.0694	0.2034	0.9074	0.0125	1.3598
11386	0.7607	0.0092	0.4021	3.6116	0.2100	0.8730	0.0321	0.0403
11387	0.5065	0.0075	0.3071	4.7324	0.0943	0.9157	0.0171	1.5532
11388	0.5324	0.0076	0.4222	4.3248	0.2061	1.0470	0.0124	1.4893
11389	0.4941	0.0073	0.3621	4.4523	0.1554	0.9393	0.0146	1.4125
11390	0.4928	0.0	0.4001	4.1176	0.1417	0.8950	0.0147	1.2039
11391	0.4764	0.0059	0.4204	5.1924	0.1868	1.0599	0.0143	1.3766
11392	0.4543	0.0074	0.3890	4.8499	0.2028	0.9134	0.0	1.1906
11393	0.5244	0.0079	0.3584	5.4645	0.1970	1.03	0.0	1.4391
11394	0.4657	0.0049	0.3341	4.1446	0.1628	0.904	0.0148	1.2962
11395	0.4338	0.0064	0.3413	3.5826	0.1676	0.8530	0.0149	1.3139
11396	0.4122	0.0066	0.3115	4.2423	0.1714	0.8224	0.0156	1.2554
11397	0.4474	0.0063	0.3170	3.9888	0.2493	0.8278	0.0186	1.2390
11398	0.4096	0.0072	0.3475	4.5795	0.1740	1.0655	0.0159	1.4417
11399	0.3796	0.0047	0.3889	4.1032	0.1853	0.7818	0.0123	1.2455
11400	0.4613	0.0050	0.3515	4.0551	0.1702	0.9107	0.0141	1.4504
11401	0.6220	0.0070	0.4064	4.0403	0.1572	0.8858	0.0173	1.6400
11402	0.4515	0.0055	0.3182	4.0531	0.1743	0.9551	0.0139	1.2747
11403	0.5034	0.0047	0.3806	4.0171	0.1811	0.8766	0.0131	1.4396
11404	0.4934	0.0042	0.3294	4.2011	0.1648	0.9961	0.0133	1.3964
11405	0.4764	0.0055	0.3557	4.1279	0.1904	0.8327	0.0132	1.2838
11406	0.4340	0.0044	0.3754	3.9745	0.1848	0.8760	0.0133	1.2134
11407	0.4444	0.0056	0.3231	3.5650	0.1789	0.9444	0.0119	1.3447
N	32	31	32	32	32	32	30	32
MEAN	0.4787	0.0062	0.3623	4.2620	0.1835	0.9291	0.0153	1.3256
S.D.	0.0734	0.0014	0.0416	0.4456	0.0343	0.0881	0.0036	0.2634
S.E.	0.0130	0.0002	0.0073	0.0788	0.0061	0.0156	0.0007	0.0466

TABLE I-D-9 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 4 - 3000 ppm

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11440	0.4746	0.0060	0.3616	3.4509	0.1535	0.8133	0.0141	1.3493
11441	0.4657	0.0053	0.3548	4.0308	0.1757	0.9575	0.0158	1.3821
11442	0.4244	0.0061	0.4334	4.9294	0.1704	0.8842	0.0134	1.2431
11443	0.4460	0.0067	0.3184	3.7853	0.1791	0.9045	0.0174	1.3893
11444	0.4744	0.0	0.3836	4.1718	0.2301	0.9559	0.0193	1.3509
11445	0.4678	0.0070	0.3923	3.5545	0.1591	0.8955	0.0140	1.2461
11446	0.7654	0.0112	0.6024	5.8300	0.3494	1.5775	0.0241	2.1071
11447	0.6996	0.0129	0.5964	4.5091	0.2073	1.2130	0.0353	0.8424
11448	0.4153	0.0134	0.4000	4.0614	0.2045	1.0302	0.0297	0.5267
11449	0.4104	0.0055	0.3331	4.1614	0.1842	0.9448	0.0137	1.3859
11450	0.5064	0.0067	0.3625	4.3209	0.1800	0.9775	0.0186	1.4598
11451	0.4454	0.0074	0.4532	5.0590	0.2267	1.0475	0.0143	1.3630
11454	0.4963	0.0057	0.3389	4.4446	0.1989	0.8653	0.0205	1.3864
11453	0.4567	0.0065	0.3445	4.9534	0.1739	0.9733	0.0135	1.2984
11455	0.5511	0.0066	0.4524	4.3148	0.2720	1.0545	0.0167	1.3987
11456	0.5393	0.0070	0.4105	4.3920	0.2801	1.0412	0.0143	1.4223
11457	0.5319	0.0092	0.4345	4.4707	0.2059	1.0461	0.0	1.6894
11459	0.5044	0.0066	0.4153	3.8062	0.2173	0.8612	0.0174	1.4563
11460	0.4444	0.0069	0.3410	4.9530	0.1827	0.8805	0.0168	1.2595
11461	0.4614	0.0061	0.3188	5.1297	0.2549	1.0541	0.0212	1.3479
11462	0.5142	0.0085	0.4005	5.2171	0.1922	0.9431	0.0161	1.4302
11463	0.3945	0.0039	0.3721	3.8890	0.1842	0.8167	0.0152	1.2775
11464	0.4302	0.0058	0.3889	4.3280	0.1836	0.9845	0.0130	1.3225
11465	0.4223	0.0047	0.3715	4.4331	0.2129	0.8984	0.0096	1.6098
11466	0.4704	0.0051	0.3284	4.2571	0.1937	0.8711	0.0120	1.2880
11467	0.5040	0.0058	0.3835	5.4705	0.2178	1.1110	0.0146	1.4554
11468	0.4424	0.0063	0.3398	4.8873	0.1851	1.0254	0.0155	1.3107
11469	0.4744	0.0035	0.4010	3.7903	0.1530	0.9264	0.0122	1.1789
11470	0.4241	0.0101	0.3648	4.2587	0.2031	0.9498	0.0153	1.3734
N	29	28	29	29	29	29	28	29
MEAN	0.5030	0.0070	0.3934	4.4781	0.2049	0.9429	0.0169	1.3500
S.D.	0.1118	0.0024	0.0584	0.6430	0.0418	0.1459	0.0054	0.2549
S.E.	0.0208	0.0005	0.0127	0.1263	0.0078	0.0271	0.0010	0.0473

TABLE I-D-9 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 1 - CONTROL

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11280	0.6604	0.0094	0.3490	3.7633	0.2212	0.8641	0.0339	0.0522
11281	0.6531	0.0105	0.4526	4.3439	0.2825	0.9368	0.0	0.1368
11282	0.6415	0.0109	0.0	4.0478	0.2344	0.9490	0.0417	0.0599
11283	0.7407	0.0113	0.4372	4.0270	0.1872	0.9634	0.0338	0.0419
11284	0.6493	0.0123	0.4571	3.3497	0.2483	0.8222	0.0318	0.0552
11285	0.5454	0.0073	0.4272	3.2868	0.1613	0.8200	0.0347	0.0534
11286	0.7148	0.0068	0.3924	3.3684	0.2076	0.8548	0.0	0.0488
11287	0.6545	0.0070	0.3418	3.7492	0.2124	0.8120	0.0326	0.0595
11288	0.7475	0.0065	0.3591	3.5870	0.2075	0.8292	0.0282	0.0395
11289	0.6412	0.0089	0.4294	3.7411	0.2372	0.9481	0.0	0.0548
11290	0.6223	0.0075	0.3547	4.7458	0.2433	0.9845	0.0360	0.0589
11291	0.7329	0.0137	0.5276	4.6409	0.2490	0.8943	0.0389	0.0482
11292	0.7233	0.0116	0.4079	4.3265	0.2135	0.9512	0.0391	0.0693
11293	0.6106	0.0081	0.4449	4.7966	0.2749	0.8664	0.0336	0.0502
11294	0.6611	0.0088	0.4775	4.1394	0.1939	0.8578	0.0390	0.0534
11295	0.6576	0.0090	0.4321	4.6933	0.2058	0.9442	0.0404	0.0395
11296	0.6582	0.0078	0.4675	3.9037	0.2130	0.8645	0.0313	0.0579
11297	0.6442	0.0067	0.3765	3.1836	0.2025	0.8349	0.0336	0.0550
11298	0.5115	0.0119	0.5032	3.6391	0.2142	0.7538	0.0277	0.0569
11299	0.0	0.0079	0.3231	3.1856	0.2454	0.7939	0.0354	0.0607
11300	0.6046	0.0058	0.3734	3.9100	0.1739	0.9502	0.0411	0.0361
11301	0.6403	0.0096	0.4611	3.9231	0.2061	0.9079	0.0367	0.0467
11302	0.6704	0.0108	0.3609	3.8333	0.2544	0.8892	0.0359	0.0571
11303	0.6345	0.0095	0.4034	3.4776	0.2142	0.8466	0.0306	0.0668
11304	0.7764	0.0110	0.3985	4.3145	0.2185	1.0188	0.0372	0.0064
11305	0.6503	0.0096	0.3983	3.5088	0.2088	0.8544	0.0280	0.0699
11306	0.6749	0.0110	0.4119	3.6674	0.2084	0.9115	0.0419	0.0656
11307	0.7404	0.0094	0.4629	4.2113	0.2109	0.9736	0.0335	0.0550
11308	0.6489	0.0089	0.3647	4.2438	0.2269	0.9531	0.0296	0.0275
11309	0.6241	0.0131	0.3422	4.4290	0.2322	0.8792	0.0306	0.0657
11310	0.6519	0.0089	0.3227	3.8737	0.1818	0.9385	0.0343	0.0599
11311	0.6422	0.0089	0.4109	4.2659	0.2384	0.8961	0.0411	0.0516
MEAN	0.6574	0.0094	0.4139	3.9430	0.2198	0.8926	0.0349	0.0550
S.D.	0.0558	0.0020	0.0516	0.4587	0.0271	0.0527	0.0043	0.0196
S.E.	0.0100	0.0004	0.0093	0.0811	0.0048	0.0111	0.0008	0.0035

TABLE I-D-9 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 2 - 300 ppm

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11344	0.7134	0.0088	0.3882	0.0	0.2132	0.8733	0.0290	0.0357
11345	0.8000	0.0077	0.3672	3.4819	0.1952	0.8306	0.0284	0.0513
11346	0.8048	0.0134	0.4330	3.3367	0.2508	0.8113	0.0269	0.0460
11347	0.6937	0.0092	0.4161	3.4782	0.2089	0.9326	0.0275	0.0479
11348	0.7053	0.0101	0.3846	3.9689	0.2154	0.9026	0.0338	0.0421
11349	0.7774	0.0068	0.3655	3.2474	0.2132	0.8932	0.0329	0.0370
11350	0.6584	0.0094	0.3675	3.5090	0.2150	0.7917	0.0275	0.0425
11351	0.6545	0.0090	0.4072	4.4201	0.2054	0.9284	0.0323	0.0452
11352	0.7040	0.0098	0.3929	3.8258	0.2302	0.9609	0.0351	0.0409
11353	0.6444	0.0119	0.3960	3.6784	0.2225	0.9073	0.0276	0.0481
11354	0.7045	0.0103	0.3326	3.4277	0.1777	0.9504	0.0295	0.0469
11355	0.7262	0.0082	0.3854	4.1431	0.2318	0.9678	0.0403	0.0528
11356	0.7130	0.0108	0.3821	4.1363	0.2457	1.0184	0.0314	0.0614
11357	0.6310	0.0086	0.4407	3.6093	0.2280	0.9000	0.0310	0.0590
11358	0.6217	0.0086	0.3791	4.2357	0.2283	0.8795	0.0274	0.0339
11359	0.6559	0.0090	0.3642	0.0	0.2372	0.9374	0.0313	0.1411
11360	0.6821	0.0120	0.4150	4.0991	0.2389	0.9107	0.0338	0.0521
11361	0.7033	0.0110	0.3262	3.4452	0.2200	0.8276	0.0314	0.0414
11362	0.6653	0.0075	0.5314	3.4310	0.2259	0.7812	0.0310	0.0598
11363	0.7238	0.0081	0.4157	4.0337	0.2502	0.9951	0.0333	0.0442
11364	1.0101	0.0195	0.5374	5.1674	0.2658	1.2108	0.0409	0.1108
11365	0.7649	0.0081	0.4412	2.7905	0.1943	0.8412	0.0299	0.0318
11366	0.6460	0.0054	0.3615	3.1841	0.2552	0.7937	0.0230	0.0372
11367	0.6502	0.0094	0.4489	3.3575	0.2159	0.8712	0.0305	0.0468
11368	0.6624	0.0094	0.4044	4.6390	0.2229	0.8958	0.0371	0.0496
11369	0.5754	0.0094	0.4072	3.3349	0.1717	0.8073	0.0366	0.0464
11370	0.7610	0.0090	0.3955	3.7696	0.2304	0.8607	0.0378	0.0572
11371	0.6361	0.0091	0.4700	3.7114	0.2315	0.8054	0.0278	0.0494
11371	0.4755	0.0066	0.3263	5.0700	0.1794	0.9812	0.0141	1.3327
11372	0.7175	0.0080	0.4580	4.1387	0.2134	0.9286	0.0353	0.0597
11373	0.6962	0.0097	0.4545	4.1316	0.2557	0.8468	0.0401	0.0700
11374	0.6127	0.0083	0.3913	3.6757	0.2217	0.8330	0.0326	0.0663
11375	0.7016	0.0108	0.5165	3.8133	0.2209	0.8333	0.0365	0.0594
J	33	33	33	31	33	33	33	33
MEAN	0.6374	0.0095	0.4109	3.8176	0.2222	0.8942	0.0316	0.0923
S.D.	0.0854	0.0024	0.0545	0.5326	0.0223	0.0851	0.0053	0.2237
S.E.	0.0149	0.0004	0.0095	0.0957	0.0039	0.0148	0.0009	0.0389

TABLE I-D-9 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 3 - 1000 ppm

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11408	0.5366	0.0081	0.3437	3.6092	0.2385	0.8159	0.0297	0.0505
11409	0.6561	0.0069	0.4259	3.3823	0.1812	0.8295	0.0249	0.0465
11410	0.6439	0.0104	0.3546	3.2329	0.2068	0.8398	0.0253	0.0269
11411	0.7572	0.0072	0.4009	3.6441	0.1982	0.8590	0.0387	0.0486
11412	0.6663	0.0108	0.3825	4.4737	0.2179	0.8805	0.0	0.0590
11413	0.6480	0.0082	0.3533	3.4195	0.2145	0.8980	0.0336	0.0566
11414	0.6939	0.0074	0.4630	3.8248	0.1852	0.9904	0.0348	0.0596
11415	0.7239	0.0096	0.4046	3.4995	0.2528	0.9624	0.0349	0.0436
11416	0.6685	0.0104	0.4011	3.7178	0.2202	0.9616	0.0400	0.0488
11417	0.6961	0.0067	0.4199	4.3066	0.2399	1.0192	0.0322	0.0501
11418	0.5966	0.0079	0.3819	3.6668	0.2015	0.9064	0.0347	0.0377
11419	0.7507	0.0079	0.4452	3.3782	0.2061	0.8426	0.0332	0.0472
11420	0.6665	0.0074	0.4436	3.6505	0.2187	0.8887	0.0312	0.0656
11421	0.7350	0.0102	0.3990	3.1176	0.2428	0.8779	0.0	0.0515
11422	0.7744	0.0	0.4466	3.7375	0.2426	0.9397	0.0382	0.0884
11423	0.7454	0.0106	0.3753	3.4698	0.2233	0.9462	0.0273	0.0550
11424	0.6836	0.0091	0.4392	4.0280	0.2379	0.9078	0.0341	0.0539
11425	0.6451	0.0067	0.3966	4.4265	0.2272	0.9675	0.0343	0.0593
11426	0.6381	0.0065	0.3763	3.8125	0.2039	0.8007	0.0279	0.0283
11427	0.5227	0.0089	0.3466	3.6717	0.1951	0.8000	0.0287	0.0498
11428	0.6218	0.0061	0.4095	4.1683	0.2202	0.8630	0.0340	0.0756
11429	0.6710	0.0069	0.3545	3.9672	0.2418	0.9254	0.0377	0.0537
11430	0.6591	0.0086	0.4358	4.3142	0.2397	0.9052	0.0435	0.0720
11431	0.6346	0.0117	0.4492	3.6329	0.2133	0.8683	0.0321	0.0571
11432	0.6737	0.0082	0.3519	3.8547	0.2099	0.9374	0.0288	0.0844
11433	0.6844	0.0095	0.3990	4.2895	0.2078	0.9095	0.0314	0.0384
11434	0.7284	0.0087	0.3619	4.0092	0.2679	0.9271	0.0358	0.0651
11435	0.6794	0.0069	0.3535	4.4302	0.2934	0.8713	0.0242	0.0308
11436	0.6553	0.0045	0.3831	4.0372	0.2385	0.8645	0.0341	0.0630
11437	0.6205	0.0050	0.3713	3.5066	0.1857	0.7891	0.0310	0.0380
11438	0.6825	0.0096	0.4281	4.0340	0.2221	0.8429	0.0414	0.0544
11439	0.6955	0.0118	0.3859	4.1351	0.2243	0.9242	0.0375	0.0446
N	32	31	32	32	32	32	30	32
MEAN	0.6730	0.0085	0.4009	3.8265	0.2225	0.8957	0.0333	0.0533
S.D.	0.0588	0.0017	0.0496	0.3678	0.0243	0.0558	0.0046	0.0144
S.E.	0.0104	0.0003	0.0072	0.0650	0.0043	0.0099	0.0008	0.0025

TABLE I-D-9 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 4 - 3000 ppm

DIMP

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11472	0.6621	0.0062	0.3362	3.4185	0.2030	0.7799	0.0233	0.0532
11473	0.6679	0.0076	0.3510	3.7771	0.2153	0.8815	0.0	0.0478
11474	0.7274	0.0094	0.3447	3.7299	0.1873	0.9509	0.0341	0.0333
11475	0.4764	0.0083	0.4233	3.6824	0.2152	0.9357	0.0348	0.0560
11476	0.7024	0.0100	0.4184	4.2275	0.2415	1.0140	0.0299	0.0669
11477	0.7965	0.0116	0.4398	4.3354	0.2078	0.9729	0.0333	0.0561
11478	0.7330	0.0086	0.4640	4.3305	0.2394	1.0167	0.0281	0.0491
11479	0.7220	0.0062	0.3720	3.6222	0.2298	0.8843	0.0368	0.0527
11480	0.5740	0.0076	0.4204	4.0224	0.2156	0.8636	0.0276	0.0552
11481	0.6407	0.0110	0.4719	3.8135	0.2404	0.9540	0.0331	0.0477
11482	0.7410	0.0100	0.3734	3.4725	0.1865	0.8070	0.0275	0.0541
11483	0.5757	0.0077	0.4385	4.0202	0.2150	0.8607	0.0267	0.0595
11484	0.6567	0.0093	0.3409	3.7356	0.2498	0.8757	0.0223	0.0336
11485	0.5139	0.0062	0.5060	4.2500	0.1875	1.0054	0.0131	1.3310
11486	0.5807	0.0071	0.4513	3.5841	0.2059	0.9526	0.0283	0.0412
11487	0.6710	0.0074	0.4010	3.6571	0.2001	0.8880	0.0308	0.0551
11488	0.9354	0.0128	0.5737	4.8620	0.2544	0.9771	0.0290	0.0741
11489	0.7171	0.0124	0.4318	3.6030	0.2552	0.7721	0.0236	0.0513
11490	0.7375	0.0100	0.4184	3.5666	0.2557	0.8404	0.0290	0.0476
11491	0.7254	0.0107	0.3492	4.0005	0.2772	0.9584	0.0234	0.0462
11492	0.6595	0.0062	0.3694	3.9483	0.2398	0.8270	0.0317	0.0587
11493	0.7625	0.0093	0.3801	3.5880	0.2102	0.9537	0.0324	0.0301
11494	0.6547	0.0133	0.3504	3.7454	0.2125	0.7854	0.0229	0.0554
11495	0.5410	0.0097	0.3739	3.8401	0.1950	0.9239	0.0283	0.0457
11496	0.6424	0.0088	0.3796	3.7074	0.1766	0.8253	0.0283	0.0525
11497	0.5472	0.0120	0.3412	4.3476	0.2345	0.9631	0.0273	0.0397
11498	0.6134	0.0089	0.5179	4.0533	0.2148	0.7630	0.0265	0.0922
11499	0.5503	0.0086	0.4215	4.3997	0.2420	0.8701	0.0296	0.0457
11500	0.6776	0.0073	0.3557	4.5674	0.2260	0.9350	0.0309	0.0329
11501	0.6383	0.0	0.4424	4.8914	0.1971	0.9079	0.0352	0.0452
11502	0.5067	0.0073	0.4774	5.4624	0.1726	0.9165	0.0153	1.4004
11503	0.7845	0.0101	0.5904	4.7868	0.2180	0.9311	0.0	0.0675
N	32	31	32	32	32	32	30	32
MEAN	0.6665	0.0092	0.4146	4.0341	0.2196	0.8994	0.0281	0.1337
S.D.	0.0956	0.0020	0.0562	0.4854	0.0258	0.0725	0.0054	0.3235
S.E.	0.0164	0.0004	0.0117	0.0858	0.0046	0.0128	0.0010	0.0572

KEY FOR INCIDENCE TABLES

+ = Present  
1 = Minimal  
2 = Mild  
3 = Moderate  
4 = Marked  
o = Tissue Missing  
N/A = Nonapplicable  
- = Negative

TABLE I-D-10

## 90-DAY TOXICITY STUDY IN RATS

## DIMP

## INCIDENCE OF HISTOLOGIC FINDINGS

Group No.	1 - Male				1 - Female				4 - Male				4 - Female							
Animal No.	11264	11265	11268	11269	11278	11293	11303	11309	11310	11311	11454	11460	11462	11470	11471	11482	11489	11490	11492	11494
Tissue Findings																				
Thyroid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ultimobronchial rest	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-
Lung																				
Interstitial pneumonia	2	3	4+	4	1	1	3	2	1		4	2	4	4	4	4	2	2	2	1
Chronic murine pneumonia																				
Heart	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Focal myocarditis																				
Focal myocardial degeneration					1															
Mesenteric Lymph Nodes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	0	-
Follicular hyperplasia																				
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Microgranulomas																	1			
Spleen	1	1	2	2	2	1	2	2	2	2	1	2	1	1	2	2	2	2	2	2
Hemosiderosis																				
Pancreas	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nematodiasis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE I-D-10 (Continued)

## 90-DAY TOXICITY STUDY IN RATS

## DIMP

## INCIDENCE OF HISTOLOGIC FINDINGS (Continued)

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
Animal No.	11264	11265	11268	11269	11278	11293	11303	11309	11310	11311	11454	11460	11462	11470	11471	11482	11489	11490	11492	11494
Tissue Findings																				
Kidneys	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Focal tubular hyperplasia																				
Tubular casts			+																	
Glomerulosclerosis																				
Peripelvic inflammation																				
Focal mineralization																				
Adrenal Glands	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cortical nodule, zona glomerulosa																				
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Testes with Epididymis	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-	-
Ovaries	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Uterus	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Predecidual reaction						+	+	+	+	+										
Hydrometra																				
Prostate	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Chronic interstitial prostatitis											+	-	-	-	-	-	-	-	-	-
Seminal Vesicles	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Granulocytic hyperplasia																		+		
Brain	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thoracic Spinal Cord	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rib Junction	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eye	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nerve with Skeletal Muscle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

PART I - SECTION E  
90-DAY TOXICITY STUDY IN MICE

DIMP

LBI PROJECT NO. 2564

SUMMARY

No evidence of toxicity resulted from dietary administration of DIMP to mice at levels of 210, 700, and 2100 ppm for 90 days.

1. OBJECTIVE

The purpose of this study was to characterize the subchronic toxicity of DIMP when incorporated in the diet of mice.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in mice of the ICR Swiss Albino strain obtained from Flow Laboratories, Rockville, Maryland, with body weights averaging 19.6 grams for males and 17.8 grams for females at initiation.

B. Animal Groups

The mice were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	30	30	Zero - Control
2	30	30	Low - 210 ppm
3	30	30	Medium - 700 ppm
4	29	30	High - 2100 ppm

They were housed in solid-bottom cages in groups of five.

### 3. EXPERIMENTAL DESIGN (Continued)

#### C. Diet Preparation

The mice were fed Purina Rodent Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

#### D. Observations

Body weights and food consumption were recorded weekly for each cage group. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects. Entries were made in records only when abnormalities were noted.

#### E. Terminations

All surviving mice were killed at 13 weeks except for 10/sex/dosage. Half of each of these subgroups was kept two weeks and half four weeks on control diet to evaluate possible recovery.

#### F. Postmortem Examinations

Each animal was subjected to a gross necropsy and any observed abnormalities were recorded. The organs listed below were weighed:

heart	kidneys	adrenals (after fixation)
liver	gonads	thyroid (after fixation)
spleen		

Suitable samples of the following organs were preserved in 10% neutral formalin:

brain	stomach	ovaries
pituitary	pancreas	uterus
thyroid	small intestine	bone marrow
lung	large intestine	urinary bladder
heart	mesenteric lymph	thoracic spinal cord
liver	node	eye
spleen	nerve with muscle	rib junction
kidneys	testes with	any unusual lesions
adrenals	epididymis	
	seminal vesicles	

### 3. EXPERIMENTAL DESIGN (Continued)

#### G. Histopathologic Examination

The tissues listed below were examined microscopically from five male and five female mice in the control and the high level test groups. Those tissues showing abnormalities at the high dosage were also examined from animals of the lower dosage groups.

brain	kidneys	mesenteric lymph node
pituitary	adrenals	testes or ovaries
thyroid	stomach	uterus or prostate
heart	pancreas	bone marrow
liver	small intestine	urinary bladder
spleen	large intestine	any unusual lesions

### 4. RESULTS

#### A. Drug Administration

No difficulty was encountered with the preparation of the diets according to plan.

#### B. Observations

Two deaths occurred in the medium level male group, one in Week 8 and one in Week 10. Several mice were discarded when it was discovered they had been missexed, and a few escaped. The net mortality attributable to treatment was:

<u>Group</u>	<u>Dietary Level</u> ppm	<u>Males</u>	<u>Females</u>
1	0	0/28 (2 ESC)	0/29 (1 Missex)
2	210	0/27 (3 ESC)	0/30
3	700	2/30	0/30
4	2100	0/29	0/30

Other signs of toxicity were not noted. This is judged not to be an important degree of mortality.

#### 4. RESULTS (Continued)

##### B. Observations (Continued)

The average values for body weights for each sex/dose group are presented in Table I-E-11. Because of the group housing plan, weights of individual mice were not recorded. The tabulated values are averages per mouse for each cage (5). Conventional statistical analysis techniques do not apply, but it seems clear that growth was alike in all groups.

Food consumption values are presented similarly in Table I-E-12. The values again are averages per mouse for each cage (5) expressed as grams/day. No differences from controls were seen.

##### C. Recovery Phase

The two- and four-week recovery phases of the study proved to be noncontributory. Since no toxic effects developed, no "recovery" could be expected.

##### D. Postmortem Examination

The weights of various organs collected at terminal necropsy are presented in Table I-E-13 as recorded and in Table I-E-14 recalculated as organ to body weight ratios. Most of the indicated differences between groups in the original data disappear in the ratio tabulation.

##### E. Histopathologic Examination

The tissues listed in 3G above were processed in the conventional manner for preparation of sections stained with hematoxylin and eosin for examination by a staff pathologist. The pathologist's own summary is attached. No important abnormalities were noted.

#### 5. CONCLUSIONS

No evidence of toxicity resulted from dietary administration of DIMP to mice at levels of 210, 700, and 2100 ppm for 90 days.

90-DAY TOXICITY STUDY IN MICE


DIMP

LBI PROJECT NO. 2564

PATHOLOGY SUMMARY

The microscopic lesions observed in this study were those routinely encountered in rats and mice.

They appeared in all dosed groups and did not differ significantly from those seen in the controls.



F. M. Garner, D.V.M.

Veterinary Pathologist

Veterinary Sciences Division

TABLE I-E-11

BODY WEIGHTS  
(grams)

GROUP MEANS

DIMP

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16
<u>MALES</u>																
<u>1 - Control</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	28	28	28	28	28	18	10	5
MEAN	19.9	23.2	24.9	28.8	30.3	30.7	31.5	44.8	27.2	31.9	37.0	32.8	35.2	36.0	37.1	36.3
<u>2 - 210 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	27	27	27	27	27	27	10	5
MEAN	19.7	23.9	25.6	28.4	30.0	30.5	31.7	42.7	31.9	32.8	33.6	28.4	34.7	33.6	35.0	34.9
<u>3 - 700 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	30	29	28	28	28	19	10	5
MEAN	19.7	23.8	26.5	28.2	30.7	30.6	31.4	46.8	42.3	32.8	34.2	34.8	35.7	35.1	32.9	29.8
<u>4 - 2100 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	30	30	30	30	30	30	10	5
MEAN	19.0	22.5	25.6	25.1	28.5	28.8	29.5	45.5	41.0	33.4	33.4	34.6	35.3	34.0	36.8	37.7

TABLE I-E-11 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS

DIMP

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16
<u>FEMALES</u>																
<u>1 - Control</u>																
NO. WEIGHED	30	30	30	30	29	30	30	30	28	28	28	28	28	28	10	5
MEAN	17.4	20.1	20.8	23.9	25.0	31.2	25.5	39.6	26.4	27.3	30.0	25.2	28.7	28.1	28.1	31.5
<u>2 - 210 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	29	29	29	29	29	29	10	5
MEAN	18.2	20.9	21.0	23.0	25.0	24.6	24.7	39.0	26.5	27.5	28.2	27.0	28.8	29.0	29.0	28.7
<u>3 - 700 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	30	30	30	30	30	30	10	5
MEAN	17.7	20.5	21.2	22.3	25.3	24.5	25.0	40.5	35.9	27.2	27.1	28.2	29.1	27.6	30.6	30.8
<u>4 - 2100 ppm</u>																
NO. WEIGHED	30	30	30	30	30	30	30	30	30	30	30	30	30	20	10	5
MEAN	17.8	19.7	21.2	21.7	24.6	24.2	24.0	39.4	34.3	26.6	26.7	26.0	28.1	26.1	29.5	29.4

TABLE I-E-12

FOOD CONSUMPTION  
(grams per day)

## GROUP MEANS

## DIMP

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16	
<u>MALES</u>																
<u>1 - Control</u>																
NO. DETM'D	30	30	30	30	30	30	30	28	28	28	28	28	28	10	5	
MEAN	5.5	4.8	5.0	5.2	5.2	5.5	-	6.3	5.7	5.6	6.4	5.6	5.8	5.1	4.7	
<u>2 - 210 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	27	27	27	27	27	27	10	5	
MEAN	5.2	5.4	5.2	5.3	5.4	5.3	-	5.2	5.5	5.5	6.8	5.6	6.2	5.3	4.8	
<u>3 - 700 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	30	29	28	28	28	28	10	5	
MEAN	4.6	4.9	5.0	5.0	5.1	5.2	-	4.0	5.3	5.5	5.5	5.1	5.5	4.7	4.9	
<u>4 - 2100 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	30	30	30	30	20	30	5	5	
MEAN	5.2	5.2	5.5	5.3	5.4	5.7	-	4.2	5.3	5.4	5.5	5.2	5.5	5.2	5.3	

TABLE I-E-12 (Continued)

FOOD CONSUMPTION  
(grams per day)

GROUP MEANS

DIMP

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16	
<u>FEMALES</u>																
<u>1 - Control</u>																
NO. DETM'D	30	30	30	29	30	30	30	28	28	28	28	28	28	10	5	
MEAN	5.4	4.9	5.1	5.7	5.5	5.3	-	5.8	5.8	5.7	6.6	5.6	6.1	4.8	4.5	
<u>2 - 210 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	29	29	29	29	29	29	10	5	
MEAN	4.8	5.2	5.5	5.3	5.3	5.1	-	5.8	5.8	5.6	5.5	5.3	5.7	5.2	5.4	
<u>3 - 700 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	30	30	30	30	30	30	10	5	
MEAN	5.2	5.5	5.7	5.6	5.7	5.6	-	4.3	5.7	5.5	6.0	5.4	6.0	5.2	4.3	
<u>4 - 2100 ppm</u>																
NO. DETM'D	30	30	30	30	30	30	30	30	30	30	30	30	30	10	5	
MEAN	5.4	5.1	5.6	5.5	5.6	5.8	-	4.6	6.0	6.1	6.1	5.8	6.2	6.1	5.9	

TABLE I-E-13

ORGAN WEIGHTS IN MALE MICE  
(grams)

## GROUP 1 - CONTROL

## DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1073	36.2	0.0100	0.1680	2.0200	0.1330	0.6500	0.0090	0.4080
1074	35.5	0.0050	0.1910	1.8600	0.0890	0.5080	0.0080	0.3200
1075	32.7	0.0060	0.2260	2.0130	0.0870	0.6220	0.0060	0.3800
1076	34.3	0.0050	0.2410	1.9620	0.1170	0.6400	0.0050	0.3750
1077	37.0	0.0050	0.2310	2.1870	0.1160	0.7580	0.0090	0.4250
1078	36.7	0.0	0.1870	2.1830	0.1400	0.6430	0.0060	0.3210
1079	34.5	0.0020	0.2240	2.5490	0.1290	0.6720	0.0030	0.3380
1080	35.9	0.0030	0.3070	2.0120	0.0980	0.7030	0.0040	0.4310
1081	37.8	0.0040	0.2430	2.6010	0.2060	0.6270	0.0060	0.2780
1082	31.5	0.0030	0.2660	2.0410	0.0980	0.6570	0.0060	0.4820
1083	36.7	0.0	0.2510	2.1760	0.1300	0.5990	0.0040	0.4000
1084	36.8	0.0050	0.2730	2.5570	0.1710	0.6700	0.0100	0.3590
1085	26.5	0.0040	0.2100	1.6360	0.0880	0.4330	0.0	0.2730
1086	38.3	0.0010	0.2890	3.0390	0.4440	0.6990	0.0040	0.3440
1087	33.8	0.0020	0.2550	2.2460	0.1190	0.5650	0.0030	0.3620
1088	30.8	0.0	0.1630	1.4270	0.0690	0.4900	0.0050	0.3360
1089	39.5	0.0070	0.1850	2.4640	0.1770	0.6580	0.0140	0.4030
1090	31.8	0.0020	0.1410	2.0920	0.1100	0.5100	0.0030	0.3180
1091	35.0	0.0100	0.1900	2.1430	0.0860	0.5820	0.0110	0.2640
1092	31.4	0.0040	0.1850	2.0280	0.0990	0.4850	0.0030	0.4200
1095	34.0	0.0010	0.1440	1.9810	0.0950	0.6410	0.0030	0.3980
1096	38.5	0.0120	0.2090	2.5610	0.1650	0.7470	0.0100	0.2770
1097	40.8	0.0020	0.2460	2.9440	0.1990	0.8360	0.0040	0.3310
1098	39.0	0.0080	0.2350	2.3000	0.1270	0.7800	0.0090	0.4470
1099	35.3	0.0020	0.2850	2.4300	0.1500	0.6520	0.0040	0.5000
1100	39.1	0.0040	0.2430	2.5700	0.0860	0.6470	0.0060	0.5360
1101	38.2	0.0010	0.2410	2.5020	0.0660	0.6610	0.0	0.3670
1102	34.3	0.0	0.2330	2.4900	0.1340	0.6280	0.0	0.4270
N	28	24	28	28	28	28	25	24
MEAN	35.6	0.0045	0.2236	2.2505	0.1331	0.6344	0.0062	0.3757
S.D.	3.2	0.0030	0.0430	0.3591	0.0711	0.0919	0.0030	0.0691
S.E.	0.6	0.0006	0.0081	0.0679	0.0134	0.0174	0.0006	0.0131

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 2 - 210 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1137	35.5	0.0050	0.1830	2.3290	0.1060	0.5910	0.0060	0.2850
1138	37.6	0.0060	0.1810	2.5870	0.1600	0.5900	0.0090	0.4150
1139	35.9	0.0060	0.2290	2.4130	0.0820	0.6380	0.0060	0.3260
1140	35.7	0.0060	0.2110	2.4280	0.1210	0.5350	0.0080	0.3290
1141	37.2	0.0050	0.1730	2.4390	0.1230	0.5870	0.0060	0.3660
1142	38.2	0.0040	0.3040	2.5470	0.1560	0.7690	0.0060	0.3830
1143	31.7	0.0040	0.3160	2.0320	0.1830	0.6510	0.0050	0.3440
1144	35.0	0.0030	0.2420	1.8130	0.0910	0.5280	0.0040	0.3780
1145	33.2	0.0040	0.2580	2.0910	0.1070	0.6070	0.0050	0.3990
1146	28.3	0.0040	0.3390	2.5360	0.1270	0.6430	0.0050	0.3430
1147	34.9	0.0030	0.2000	1.9290	0.1110	0.5600	0.0080	0.3330
1148	34.5	0.0030	0.1960	1.8890	0.1250	0.6810	0.0050	0.3200
1149	34.8	0.0040	0.1810	2.3560	0.1160	0.6460	0.0	0.3470
1150	35.4	0.0	0.1960	2.2410	0.1040	0.6370	0.0080	0.3560
1151	35.8	0.0040	0.1690	2.2080	0.1570	0.7470	0.0080	0.3330
1152	28.3	0.0090	0.1650	1.7790	0.0520	0.4860	0.0040	0.2780
1153	32.4	0.0090	0.2350	2.2380	0.1050	0.5620	0.0080	0.2810
1154	33.5	0.0070	0.2360	2.3260	0.0740	0.6910	0.0060	0.3220
1155	35.5	0.0040	0.2580	2.4190	0.0790	0.6290	0.0050	0.2790
1156	31.6	0.0030	0.2230	2.0120	0.1020	0.5150	0.0070	0.3250
1157	34.3	0.0020	0.2820	2.3290	0.1540	0.6820	0.0	0.4130
1158	35.1	0.0030	0.2790	2.5580	0.1360	0.6300	0.0080	0.3560
1159	36.8	0.0030	0.2500	2.2890	0.1160	0.6810	0.0050	0.3880
1160	36.4	0.0	0.2980	2.6290	0.1170	0.6760	0.0030	0.5290
1161	37.6	0.0020	0.2640	2.4120	0.0850	0.5640	0.0050	0.4110
1165	38.1	0.0020	0.2570	2.7670	0.1340	0.8280	0.0030	0.4510
1166	37.4	0.0020	0.2490	2.6940	0.1200	0.8010	0.0030	0.4470
N	27	25	27	27	27	27	25	27
MEAN	34.8	0.0043	0.2359	2.3070	0.1164	0.6354	0.0058	0.3606
S.D.	2.8	0.0020	0.0479	0.2672	0.0296	0.0851	0.0018	0.0588
S.E.	0.5	0.0004	0.0092	0.0514	0.0057	0.0164	0.0004	0.0113

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 3 - 700 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
1201	34.3	0.0	0.1590	2.1450	0.0890	0.6850	0.0060	0.3690
1202	37.7	0.0020	0.2330	2.7620	0.1850	0.6470	0.0050	0.3190
1203	34.1	0.0040	0.2300	2.4300	0.6620	0.7230	0.0090	0.3340
1204	34.4	0.0050	0.2090	2.5290	0.2080	0.5630	0.0070	0.3480
1205	40.7	0.0030	0.1920	2.8560	0.2130	0.7720	0.0	0.3700
1206	37.6	0.0040	0.1550	1.9600	0.1090	0.5900	0.0070	0.4500
1208	34.5	0.0060	0.2220	1.9160	0.1250	0.6130	0.0	0.3740
1209	35.6	0.0030	0.2030	1.8050	0.1280	0.5850	0.0040	0.3020
1210	34.7	0.0040	0.2040	2.0470	0.0910	0.6560	0.0040	0.2400
1211	36.5	0.0050	0.1980	2.2720	0.1690	0.5780	0.0050	0.3510
1212	30.8	0.0060	0.1490	2.0170	0.1630	0.4550	0.0080	0.3350
1213	37.9	0.0050	0.2040	2.5040	0.4250	0.7400	0.0	0.3140
1214	34.0	0.0040	0.1790	2.5830	0.1460	0.7100	0.0070	0.3340
1215	41.6	0.0050	0.2010	2.8460	0.0990	0.6790	0.0070	0.4080
1217	36.7	0.0040	0.2470	2.4520	0.1840	0.7490	0.0060	0.3290
1218	39.6	0.0030	0.3700	2.9550	0.1050	0.7350	0.0060	0.3250
1219	42.1	0.0060	0.3840	2.9900	0.1300	0.7510	0.0090	0.3620
1220	34.3	0.0040	0.1750	2.4460	0.0920	0.6520	0.0060	0.3960
1221	34.6	0.0	0.2010	1.9950	0.1190	0.5770	0.0080	0.3940
1222	35.0	0.0050	0.2250	2.3090	0.1210	0.5200	0.0800	0.3420
1223	33.6	0.0040	0.1180	2.4070	0.0940	0.5580	0.0060	0.3730
1224	37.2	0.0040	0.1830	2.0950	0.0870	0.5260	0.0060	0.3150
1225	33.9	0.0030	0.1820	2.2920	0.1060	0.5630	0.0	0.3360
1226	34.2	0.0020	0.1870	2.0800	0.1000	0.6800	0.0040	0.4150
1227	37.8	0.0040	0.2970	2.7100	0.1210	0.6260	0.0060	0.3800
1228	38.8	0.0050	0.2680	3.1420	0.1280	0.8540	0.0050	0.4900
1229	33.7	0.0	0.2370	2.4900	0.1040	0.6750	0.0050	0.3840
1230	36.9	0.0040	0.2760	2.7680	0.0930	0.7880	0.0070	0.4600
N	28	25	28	28	28	28	24	28
MEAN	36.2	0.0042	0.2174	2.4215	0.1570	0.6518	0.0093	0.3625
S.D.	2.7	0.0011	0.0596	0.3627	0.1194	0.0938	0.0151	0.0520
S.E.	0.5	0.0002	0.0113	0.0685	0.0226	0.0177	0.0031	0.0098

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 4 - 2100 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1265	39.4	0.0050	0.1810	2.9730	0.0980	0.6450	0.0	0.3630
1266	34.5	0.0060	0.1780	2.6930	0.1270	0.8140	0.0	0.2980
1267	39.9	0.0040	0.1650	2.8650	0.1200	0.6740	0.0	0.5090
1268	36.9	0.0040	0.1430	2.5670	0.0360	0.6410	0.0	0.3890
1269	38.7	0.0040	0.1500	2.7500	0.1950	0.7980	0.0060	0.3340
1270	34.6	0.0030	0.2600	1.9780	0.1470	0.7300	0.0	0.4720
1271	34.7	0.0020	0.2070	2.6250	0.1340	0.7070	0.0040	0.3470
1272	40.7	0.0050	0.3330	2.9710	0.1670	0.6900	0.0060	0.5200
1273	36.4	0.0030	0.1930	2.2720	0.1260	0.7250	0.0050	0.4670
1274	36.0	0.0030	0.1450	2.3110	0.0840	0.6300	0.0030	0.4140
1275	36.6	0.0040	0.2020	2.3050	0.0830	0.5910	0.0060	0.3610
1276	31.9	0.0040	0.1620	1.7560	0.1180	0.4840	0.0050	0.4140
1277	36.5	0.0030	0.1560	2.4990	0.1690	0.6300	0.0060	0.2470
1278	35.2	0.0040	0.1520	2.1540	0.0220	0.5840	0.0060	0.2800
1279	42.1	0.0030	0.2070	3.1390	0.1130	0.8590	0.0080	0.3280
1280	37.3	0.0050	0.2340	2.8320	0.1200	0.7550	0.0080	0.3540
1281	38.5	0.0040	0.2710	2.9050	0.1440	0.6970	0.0080	0.3830
1282	41.8	0.0050	0.2540	3.1380	0.1170	0.7250	0.0	0.4400
1283	37.2	0.0010	0.1970	2.4770	0.1140	0.6590	0.0040	0.3730
1284	36.2	0.0	0.2080	2.5140	0.1840	0.6720	0.0080	0.3730
1285	25.5	0.0080	0.1840	1.7070	0.1100	0.4810	0.0060	0.3840
1286	38.2	0.0070	0.2810	3.1100	0.1010	0.6030	0.0060	0.4110
1287	31.5	0.0	0.2230	2.1400	0.0780	0.5780	0.0050	0.4070
1288	35.3	0.0120	0.2710	2.3800	0.1280	0.5430	0.0110	0.4640
1289	26.0	0.0100	0.1410	1.8900	0.0740	0.4100	0.0150	0.3590
1290	34.1	0.0030	0.1640	2.2740	0.1040	0.6370	0.0030	0.3820
1291	37.7	0.0110	0.1450	2.2860	0.0690	0.5700	0.0160	0.4280
1292	37.0	0.0110	0.1900	2.3680	0.1020	0.7510	0.0140	0.3880
1293	38.4	0.0060	0.1610	2.6730	0.1200	0.6220	0.0060	0.4820
1294	39.1	0.0030	0.2020	2.8620	0.1450	0.6320	0.0050	0.3710
N	30	28	30	30	30	30	24	30
MEAN	36.3	0.0051	0.1987	2.5138	0.1150	0.6512	0.0071	0.3914
S.D.	3.8	0.0029	0.0487	0.4003	0.0386	0.0997	0.0035	0.0638
S.E.	0.7	0.0005	0.0089	0.0731	0.0071	0.0182	0.0007	0.0117

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

## GROUP 1 - CONTROL

## DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1105	25.0	0.0040	0.1390	1.6270	0.1340	0.3790	0.0120	0.0170
1106	36.5	0.0030	0.2330	2.3830	0.1530	0.5000	0.0110	0.0140
1107	31.0	0.0040	0.2310	1.9400	0.1640	0.5210	0.0100	0.0350
1108	36.8	0.0060	0.2880	2.4980	0.1980	0.5480	0.0110	0.0260
1110	31.3	0.0030	0.2430	1.8950	0.0770	0.4570	0.0100	0.0410
1111	35.8	0.0050	0.1390	2.0440	0.1080	0.5070	0.0110	0.0110
1112	29.3	0.0040	0.1480	1.9550	0.1190	0.5220	0.0110	0.0340
1113	28.5	0.0060	0.1740	1.6290	0.1000	0.4450	0.0090	0.0340
1114	27.7	0.0040	0.1810	1.6320	0.1680	0.4410	0.0100	0.0460
1115	25.9	0.0020	0.1790	1.6570	0.1060	0.4060	0.0100	0.0160
1116	26.8	0.0030	0.1790	1.5910	0.1220	0.3590	0.0090	0.0290
1117	31.6	0.0030	0.1690	2.1110	0.1300	0.4640	0.0090	0.0270
1118	33.5	0.0080	0.1960	2.0170	0.1330	0.4870	0.0140	0.0870
1119	33.8	0.0	0.1840	2.0820	0.1470	0.5240	0.0070	0.0430
1120	25.3	0.0	0.1380	1.4260	0.0890	0.3700	0.0090	0.0230
1121	28.9	0.0	0.1380	1.9710	0.1190	0.3970	0.0100	0.0150
1122	28.5	0.0010	0.1710	1.9040	0.0880	0.4600	0.0050	0.0270
1123	30.3	0.0050	0.1770	1.7960	0.1620	0.4590	0.0180	0.0250
1124	31.0	0.0080	0.1460	2.1030	0.1150	0.4490	0.0160	0.0330
1125	28.5	0.0060	0.1160	1.7500	0.0650	0.4290	0.0090	0.0160
1126	26.3	0.0040	0.1410	1.4340	0.1050	0.3660	0.0100	0.0130
1127	29.4	0.0040	0.2190	1.8180	0.1090	0.4180	0.0110	0.0180
1128	26.2	0.0050	0.1230	1.6030	0.1040	0.3230	0.0	0.0110
1129	26.8	0.0080	0.1560	1.6570	0.1400	0.4750	0.0100	0.0180
1130	28.6	0.0110	0.1830	1.5630	0.0720	0.4450	0.0100	0.0640
1131	28.1	0.0060	0.1820	1.9690	0.1630	0.4860	0.0170	0.0350
1132	28.3	0.0070	0.1560	1.6710	0.0930	0.3450	0.0130	0.0430
1133	27.7	0.0060	0.0260	1.8070	0.1200	0.3990	0.0100	0.0380
N	28	25	28	28	28	28	27	28
MEAN	29.6	0.0050	0.1698	1.8405	0.1215	0.4422	0.0108	0.0300
S.D.	3.3	0.0022	0.0483	0.2609	0.0321	0.0596	0.0028	0.0169
S.E.	0.6	0.0004	0.0091	0.0493	0.0061	0.0113	0.0005	0.0032

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 2 - 210 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
1169	29.2	0.0080	0.1770	1.7720	0.1070	0.4290	0.0100	0.0390
1170	31.9	0.0060	0.2210	1.9080	0.1130	0.5220	0.0100	0.0330
1171	30.5	0.0030	0.2100	1.9970	0.1040	0.4770	0.0100	0.0240
1172	29.3	0.0040	0.1540	1.3180	0.0520	0.3510	0.0	0.0230
1173	30.0	0.0060	0.1600	1.8460	0.0780	0.4080	0.0090	0.0190
1174	28.1	0.0050	0.1270	1.4720	0.1690	0.3990	0.0120	0.0660
1175	26.2	0.0030	0.1320	1.3190	0.1090	0.4780	0.0100	0.0210
1176	27.1	0.0050	0.2290	1.7210	0.0800	0.4230	0.0100	0.0510
1177	30.4	0.0030	0.1670	2.0400	0.0970	0.4600	0.0120	0.0350
1178	27.9	0.0050	0.2030	1.5230	0.1090	0.4650	0.0070	0.0320
1179	24.8	0.0030	0.1020	1.2050	0.1220	0.3430	0.0050	0.0240
1180	27.9	0.0060	0.1370	1.7210	0.1070	0.4510	0.0060	0.0450
1181	29.0	0.0060	0.1260	1.9190	0.1270	0.4210	0.0090	0.0340
1182	28.0	0.0080	0.1250	1.8360	0.1300	0.4780	0.0080	0.0230
1183	26.4	0.0060	0.1320	1.7130	0.1270	0.3680	0.0	0.0350
1184	27.2	0.0080	0.1710	1.6380	0.1390	0.4080	0.0100	0.0320
1186	32.5	0.0060	0.4360	2.3830	0.3470	0.6870	0.0100	0.2570
1187	31.3	0.0050	0.2140	2.0750	0.1070	0.4320	0.0080	0.0140
1188	27.0	0.0	0.4690	1.9640	0.2990	0.6210	0.0050	0.2550
1189	28.9	0.0	0.1440	1.4250	0.1130	0.3660	0.0080	0.0490
1190	31.8	0.0	0.1860	2.1090	0.1770	0.4980	0.0070	0.0410
1191	28.8	0.0050	0.1830	2.1370	0.1070	0.5130	0.0080	0.0780
1192	28.7	0.0020	0.1410	1.7900	0.0560	0.3940	0.0	0.0360
1194	31.1	0.0040	0.2490	1.9300	0.1380	0.5110	0.0	0.0440
1195	31.8	0.0030	0.2280	2.0800	0.1300	0.4870	0.0080	0.0560
1196	28.0	0.0040	0.2150	1.6300	0.1060	0.4330	0.0070	0.0350
1197	32.3	0.0030	0.2540	2.3300	0.1270	0.5770	0.0070	0.0210
1198	23.3	0.0070	0.1550	1.2700	0.0480	0.3310	0.0080	0.0320
N	28	25	28	28	28	28	24	28
MEAN	28.9	0.0050	0.1945	1.7883	0.1259	0.4547	0.0085	0.0519
S.D.	2.3	0.0017	0.0838	0.3132	0.0634	0.0819	0.0019	0.0594
S.E.	0.4	0.0003	0.0158	0.0592	0.0120	0.0155	0.0004	0.0112

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 3 - 700 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1233	31.6	0.0090	0.1800	1.8800	0.1190	0.4650	0.0110	0.0120
1234	32.8	0.0040	0.1750	2.0780	0.0950	0.4750	0.0100	0.0250
1235	35.7	0.0050	0.2360	2.4170	0.1200	0.5480	0.0080	0.0280
1236	27.9	0.0070	0.2080	1.7630	0.0950	0.4470	0.0110	0.0130
1237	27.9	0.0060	0.1820	1.1750	0.1400	0.3910	0.0	0.0100
1238	30.2	0.0030	0.1670	1.4390	0.1480	0.3960	0.0090	0.0600
1239	33.2	0.0	0.2440	2.0060	0.1470	0.5390	0.0090	0.0450
1240	33.6	0.0030	0.2000	1.8950	0.0750	0.5280	0.0090	0.0440
1241	30.8	0.0040	0.2310	1.6230	0.1470	0.4810	0.0	0.0410
1242	27.4	0.0040	0.1810	1.4190	0.0690	0.4520	0.0080	0.0260
1243	29.0	0.0020	0.1560	1.7180	0.0890	0.4130	0.0100	0.0210
1244	26.4	0.0020	0.1520	1.8580	0.1070	0.4170	0.0110	0.0080
1245	30.6	0.0020	0.2150	2.1620	0.1310	0.4790	0.0	0.0120
1246	26.2	0.0050	0.1670	1.6980	0.1290	0.4120	0.0140	0.0130
1247	28.8	0.0070	0.2130	2.0480	0.1150	0.4690	0.0110	0.0310
1248	27.4	0.0020	0.1170	1.6840	0.1030	0.3850	0.0060	0.0010
1249	31.5	0.0030	0.1600	2.0280	0.1120	0.4600	0.0090	0.0250
1250	31.3	0.0050	0.1980	2.1140	0.1250	0.5750	0.0110	0.0290
1251	30.3	0.0040	0.1920	1.9260	0.1170	0.4610	0.0190	0.0410
1252	36.0	0.0050	0.2350	2.5250	0.1640	0.5750	0.0110	0.0590
1253	32.5	0.0060	0.2080	1.8600	0.1570	0.4820	0.0090	0.0340
1254	30.6	0.0040	0.2310	1.9360	0.0910	0.4630	0.0	0.0290
1255	27.4	0.0040	0.1580	1.5160	0.1050	0.3920	0.0090	0.0350
1256	31.4	0.0020	0.2190	2.0880	0.1380	0.5170	0.0080	0.0460
1257	25.9	0.0060	0.2100	1.3550	0.0830	0.3760	0.0110	0.0520
1258	29.0	0.0040	0.1550	1.5820	0.0790	0.4320	0.0090	0.0170
1259	28.9	0.0	0.2330	2.1140	0.1550	0.4820	0.0160	0.0220
1260	28.3	0.0030	0.1700	1.8080	0.1280	0.4280	0.0070	0.0400
1261	24.9	0.0050	0.1390	1.5340	0.0920	0.3980	0.0080	0.0100
1262	25.3	0.0040	0.1520	1.4830	0.1670	0.3910	0.0110	0.0130
N	30	28	30	30	30	30	26	30
MEAN	29.8	0.0043	0.1895	1.8244	0.1181	0.4576	0.0102	0.0281
S.D.	2.9	0.0017	0.0335	0.3116	0.0277	0.0568	0.0027	0.0158
S.E.	0.5	0.0003	0.0061	0.0569	0.0050	0.0104	0.0005	0.0029

TABLE I-E-13 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 4 - 2100 ppm

DIMP

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1297	34.2	0.0040	0.1950	2.3220	0.1270	0.4870	0.0070	0.0660
1298	30.6	0.0050	0.1450	1.7290	0.1150	0.4420	0.0120	0.0400
1299	23.2	0.0040	0.1370	1.3830	0.0730	0.3700	0.0080	0.0160
1300	30.5	0.0100	0.1670	2.1440	0.1960	0.5740	0.0190	0.0710
1301	29.7	0.0080	0.1950	1.9280	0.1120	0.4750	0.0100	0.0480
1302	29.3	0.0020	0.1660	1.6620	0.0900	0.4820	0.0040	0.0260
1303	29.8	0.0020	0.1410	1.6420	0.1180	0.5180	0.0100	0.0130
1304	31.0	0.0020	0.1470	1.6980	0.1760	0.4500	0.0060	0.0540
1305	32.5	0.0030	0.1770	1.7810	0.1000	0.4360	0.0100	0.0190
1306	32.5	0.0	0.1690	1.4390	0.1050	0.3730	0.0100	0.0400
1307	31.9	0.0050	0.0970	2.0150	0.0770	0.4890	0.0090	0.0500
1308	26.3	0.0030	0.1300	1.3720	0.1090	0.3730	0.0100	0.0280
1309	24.8	0.0030	0.1260	1.5570	0.1030	0.4110	0.0080	0.0400
1310	29.9	0.0010	0.1140	1.5620	0.1270	0.3580	0.0	0.0520
1311	29.4	0.0030	0.1780	1.8940	0.1350	0.5350	0.0110	0.0460
1312	27.1	0.0030	0.1710	1.6630	0.0930	0.3540	0.0	0.0180
1313	29.5	0.0050	0.2380	2.1380	0.1470	0.4960	0.0110	0.0140
1314	27.7	0.0030	0.2130	1.8770	0.1320	0.5000	0.0110	0.0310
1315	29.0	0.0050	0.1530	1.9980	0.1510	0.4970	0.0	0.0310
1316	31.0	0.0040	0.2190	1.8380	0.1090	0.4860	0.0100	0.0260
1317	29.4	0.0090	0.1370	1.5000	0.1070	0.3760	0.0100	0.0220
1318	28.7	0.0120	0.2280	2.2880	0.1120	0.5080	0.0090	0.0120
1319	18.0	0.0110	0.1440	1.1800	0.0840	0.2510	0.0100	0.0
1320	27.0	0.0090	0.2050	1.9620	0.0930	0.4510	0.0110	0.0230
1321	27.5	0.0070	0.1780	1.4150	0.1040	0.3880	0.0100	0.0130
1322	26.2	0.0030	0.2490	1.6330	0.1300	0.5120	0.0180	0.0180
1323	28.3	0.0050	0.1680	1.9950	0.1470	0.4710	0.0100	0.0580
1324	31.0	0.0060	0.2520	1.8540	0.1200	0.5070	0.0090	0.0380
1325	27.2	0.0030	0.1710	1.7440	0.1490	0.4700	0.0080	0.0590
1326	29.0	0.0040	0.1480	2.1650	0.1260	0.4640	0.0110	0.0360
N	30	29	30	30	30	30	27	29
MEAN	28.7	0.0050	0.1719	1.7793	0.1189	0.4501	0.0101	0.0348
S.D.	3.1	0.0029	0.0396	0.2867	0.0277	0.0690	0.0030	0.0172
S.E.	0.6	0.0005	0.0072	0.0523	0.0051	0.0126	0.0006	0.0032

TABLE I-E-14

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

## GROUP 1 - CONTROL

## DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1073	0.0276	0.4641	5.5801	0.3674	1.7956	0.0249	1.1271
1074	0.0141	0.5380	5.2394	0.2507	1.4310	0.0225	0.9014
1075	0.0143	0.6911	6.1560	0.2661	1.9021	0.0183	1.1621
1076	0.0146	0.7026	5.7201	0.3411	1.8659	0.0146	1.0933
1077	0.0135	0.6243	5.9108	0.3135	2.0486	0.0243	1.1486
1078	0.0	0.5095	5.9482	0.3815	1.7520	0.0163	0.8747
1079	0.0052	0.5818	6.6208	0.3351	1.7455	0.0078	0.8779
1080	0.0084	0.8552	5.6045	0.2730	1.9582	0.0111	1.2006
1081	0.0106	0.6429	6.8810	0.5450	1.6587	0.0159	0.7354
1082	0.0095	0.8444	6.4794	0.3111	2.0857	0.0190	1.5302
1083	0.0	0.6839	5.9292	0.3542	1.6322	0.0109	1.0899
1084	0.0136	0.7418	6.9484	0.4647	1.8207	0.0272	0.9755
1085	0.0151	0.7925	6.1736	0.3321	1.6340	0.0	1.0302
1086	0.0025	0.7546	7.9347	1.1593	1.8251	0.0104	0.8982
1087	0.0059	0.7544	6.6450	0.3521	1.6716	0.0089	1.0710
1088	0.0	0.5292	4.6331	0.2240	1.5909	0.0162	1.0909
1089	0.0177	0.4684	6.2380	0.4481	1.6658	0.0354	1.0203
1090	0.0063	0.4434	6.5786	0.3459	1.6038	0.0094	1.0000
1091	0.0286	0.5429	6.1229	0.2457	1.6629	0.0314	0.7543
1092	0.0127	0.5892	6.4586	0.3153	1.5446	0.0096	1.3376
1095	0.0029	0.4235	5.8265	0.2794	1.8853	0.0088	1.1706
1096	0.0312	0.5429	6.6519	0.4286	1.9403	0.0260	0.7195
1097	0.0049	0.6029	7.2157	0.4877	2.0490	0.0098	0.8113
1098	0.0205	0.6023	5.8944	0.3255	1.9990	0.0231	1.1456
1099	0.0057	0.8074	6.8838	0.4249	1.8470	0.0113	1.4164
1100	0.0102	0.6215	6.5729	0.2199	1.6547	0.0153	1.3708
1101	0.0026	0.6309	6.5497	0.1728	1.7304	0.0	0.9607
1102	0.0	0.6793	7.2545	0.3907	1.8309	0.0	1.2449
N	24	24	28	28	28	25	28
MEAN	0.0126	0.6309	6.3092	0.3698	1.7797	0.0171	1.0628
S.D.	0.0092	0.1213	0.6739	0.1771	0.1665	0.0078	0.2054
S.E.	0.0017	0.0229	0.1273	0.0335	0.0315	0.0016	0.0388

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 2 - 210 ppm

DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1137	0.0141	0.5155	6.5606	0.2986	1.6648	0.0169	0.8028
1138	0.0160	0.4814	6.8803	0.4255	1.5691	0.0239	1.1037
1139	0.0167	0.6379	6.7214	0.2284	1.7772	0.0167	0.9041
1140	0.0168	0.5910	6.8011	0.3389	1.4986	0.0224	0.9216
1141	0.0134	0.4651	6.5565	0.3306	1.5780	0.0161	0.9839
1142	0.0105	0.7958	6.6675	0.4084	2.0131	0.0157	1.0026
1143	0.0126	0.9968	6.4101	0.5773	2.0536	0.0158	1.0852
1144	0.0086	0.6914	5.1800	0.2600	1.5086	0.0114	1.0800
1145	0.0120	0.7771	6.2982	0.3223	1.8283	0.0151	1.2018
1146	0.0141	1.1979	8.9611	0.4488	2.2721	0.0177	1.2120
1147	0.0086	0.5731	5.5272	0.3181	1.6046	0.0229	0.9542
1148	0.0087	0.5681	5.4754	0.3623	1.9739	0.0145	0.9275
1149	0.0115	0.5201	6.7701	0.3333	1.8563	0.0	0.9971
1150	0.0	0.5537	6.3305	0.2938	1.7994	0.0226	1.0056
1151	0.0112	0.4721	6.1676	0.4385	2.0866	0.0223	0.9302
1152	0.0342	0.6274	6.7643	0.1977	1.8479	0.0152	1.0570
1153	0.0278	0.7253	6.9074	0.3241	1.7346	0.0247	0.8673
1154	0.0209	0.7045	6.9433	0.2209	2.0627	0.0179	0.9612
1155	0.0110	0.7068	6.6274	0.2164	1.7233	0.0137	0.7644
1156	0.0095	0.7057	6.3671	0.3228	1.6297	0.0222	1.0285
1157	0.0058	0.8222	6.7901	0.4490	1.9883	0.0	1.2041
1158	0.0085	0.7949	7.2877	0.3875	1.7949	0.0228	1.0142
1159	0.0082	0.6793	6.2201	0.3152	1.8505	0.0136	1.0543
1160	0.0	0.8187	7.2225	0.3214	1.8571	0.0082	1.4533
1161	0.0053	0.7021	6.4149	0.2261	1.5000	0.0133	1.0931
1165	0.0052	0.6614	7.2625	0.3517	2.1732	0.0079	1.1837
1166	0.0053	0.6658	7.2032	0.3209	2.1417	0.0080	1.1952
N	25	27	27	27	27	25	27
MEAN	0.0127	0.6834	6.6414	0.3348	1.8292	0.0169	1.0368
S.D.	0.0069	0.1621	0.6946	0.0859	0.2201	0.0051	0.1453
S.E.	0.0014	0.0312	0.1345	0.0165	0.0424	0.0010	0.0280

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 3 - 700 ppm

DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
1201	0.0	0.4636	6.2536	0.2595	1.9971	0.0175	1.0758
1202	0.0053	0.6180	7.3263	0.4907	1.7162	0.0133	0.8462
1203	0.0117	0.6745	7.1261	1.9413	2.1202	0.0264	0.9795
1204	0.0145	0.6076	7.3517	0.6047	1.6366	0.0203	1.0116
1205	0.0074	0.4717	7.0172	0.5233	1.8968	0.0	0.9091
1206	0.0106	0.4122	5.2128	0.2899	1.5691	0.0186	1.1968
1208	0.0174	0.6435	5.5536	0.3623	1.7768	0.0	1.0841
1209	0.0084	0.5702	5.0702	0.3596	1.6433	0.0112	0.8483
1210	0.0115	0.5879	5.8991	0.2622	1.8905	0.0115	0.6916
1211	0.0137	0.5425	6.2247	0.4630	1.5836	0.0137	0.9616
1212	0.0195	0.4838	6.5487	0.5292	1.4773	0.0260	1.0877
1213	0.0132	0.5383	6.6069	1.1214	1.9525	0.0	0.8285
1214	0.0118	0.5265	7.5971	0.4294	2.0882	0.0206	0.9824
1215	0.0120	0.4832	6.8413	0.2380	1.6322	0.0168	0.9808
1217	0.0109	0.6730	6.6812	0.5014	2.0409	0.0163	0.8965
1218	0.0076	0.9343	7.4621	0.2652	1.8561	0.0152	0.8207
1219	0.0143	0.9121	7.1021	0.3088	1.7838	0.0214	0.8599
1220	0.0117	0.5102	7.1312	0.2682	1.9009	0.0175	1.1545
1221	0.0	0.5809	5.7659	0.3439	1.6676	0.0231	1.1387
1222	0.0143	0.6429	6.5971	0.3457	1.4857	0.2286	0.9771
1223	0.0119	0.3512	7.1637	0.2798	1.6607	0.0179	1.1101
1224	0.0108	0.4919	5.6317	0.2339	1.4140	0.0161	0.8468
1225	0.0088	0.5369	6.7611	0.3127	1.6608	0.0	0.9912
1226	0.0058	0.5468	6.0819	0.2924	1.9883	0.0117	1.2134
1227	0.0106	0.7857	7.1693	0.3201	1.6561	0.0159	1.0053
1228	0.0129	0.6907	8.0979	0.3299	2.2010	0.0129	1.2629
1229	0.0	0.7033	7.3887	0.3086	2.0030	0.0148	1.1395
1230	0.0108	0.7480	7.5014	0.2520	2.1355	0.0190	1.2466
N	25	28	28	28	28	24	28
MEAN	0.0115	0.5975	6.6845	0.4370	1.8012	0.0261	1.0053
S.D.	0.0033	0.1360	0.7708	0.3436	0.2197	0.0433	0.1462
S.E.	0.0007	0.0257	0.1457	0.0649	0.0415	0.0088	0.0276

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 4 - 2100 ppm

DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1265	0.0127	0.4594	7.5457	0.2487	1.6371	0.0	0.9213
1266	0.0174	0.5159	7.8058	0.3681	2.3594	0.0	0.8638
1267	0.0100	0.4135	7.1804	0.3008	1.6892	0.0	1.2757
1268	0.0108	0.3875	6.9566	0.0976	1.7371	0.0	1.0542
1269	0.0103	0.3876	7.1059	0.5039	2.0620	0.0155	0.8630
1270	0.0087	0.7514	5.7168	0.4249	2.1098	0.0	1.3642
1271	0.0058	0.5965	7.5648	0.3862	2.0375	0.0115	1.0000
1272	0.0123	0.8182	7.2998	0.4103	1.6953	0.0147	1.2776
1273	0.0082	0.5302	6.2418	0.3462	1.9918	0.0137	1.2830
1274	0.0083	0.4028	6.4194	0.2333	1.7500	0.0083	1.1500
1275	0.0109	0.5519	6.2978	0.2268	1.6148	0.0164	0.9863
1276	0.0125	0.5078	5.5047	0.3699	1.5172	0.0157	1.2978
1277	0.0082	0.4274	6.8466	0.4630	1.7260	0.0164	0.6767
1278	0.0114	0.4318	6.1193	0.0625	1.6591	0.0170	0.7955
1279	0.0071	0.4917	7.4561	0.2684	2.0404	0.0190	0.7791
1280	0.0134	0.6273	7.5925	0.3217	2.0241	0.0214	0.9491
1281	0.0104	0.7039	7.5455	0.3740	1.8104	0.0208	0.9948
1282	0.0120	0.6077	7.5072	0.2799	1.7344	0.0	1.0526
1283	0.0027	0.5296	6.6586	0.3065	1.7715	0.0108	1.0027
1284	0.0	0.5746	6.9448	0.5083	1.8564	0.0221	1.0304
1285	0.0314	0.7216	6.6941	0.4314	1.8863	0.0235	1.5059
1286	0.0183	0.7356	8.1414	0.2644	1.5785	0.0157	1.0759
1287	0.0	0.7079	6.7436	0.2476	1.8349	0.0159	1.2921
1288	0.0340	0.7677	6.7422	0.3626	1.5382	0.0312	1.3144
1289	0.0385	0.5423	7.2692	0.2846	1.5769	0.0577	1.3808
1290	0.0088	0.4809	6.6686	0.3050	1.8680	0.0088	1.1202
1291	0.0292	0.3846	6.0637	0.1830	1.5119	0.0424	1.1353
1292	0.0297	0.5135	6.4000	0.2757	2.0297	0.0378	1.0486
1293	0.0156	0.4193	6.9609	0.3125	1.6198	0.0156	1.2552
1294	0.0077	0.5166	7.3197	0.3708	1.6164	0.0128	0.9488
N	28	30	30	30	30	24	30
MEAN	0.0145	0.5502	6.9121	0.3179	1.7961	0.0202	1.0898
S.D.	0.0093	0.1278	0.6302	0.1035	0.2089	0.0115	0.2014
S.E.	0.0014	0.0233	0.1151	0.0189	0.0381	0.0024	0.0368

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

## GROUP 1 - CONTROL

## DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1105	0.0160	0.5560	6.5080	0.5360	1.5160	0.0480	0.0680
1106	0.0082	0.6384	6.5288	0.4192	1.3699	0.0301	0.0384
1107	0.0129	0.7452	6.2581	0.5290	1.6806	0.0323	0.1129
1108	0.0163	0.7826	6.7840	0.5380	1.4891	0.0299	0.0707
1110	0.0096	0.7764	6.0543	0.2460	1.4601	0.0319	0.1310
1111	0.0140	0.3883	5.7095	0.3017	1.4162	0.0307	0.0307
1112	0.0137	0.5051	6.6724	0.4061	1.7816	0.0375	0.1160
1113	0.0211	0.6105	5.7158	0.3509	1.5614	0.0316	0.1193
1114	0.0144	0.6534	5.8917	0.6065	1.5921	0.0361	0.1661
1115	0.0077	0.6911	6.3977	0.4093	1.5676	0.0386	0.0618
1116	0.0112	0.6679	5.9366	0.4552	1.3396	0.0336	0.1082
1117	0.0095	0.5348	6.6804	0.4114	1.4684	0.0285	0.0854
1118	0.0239	0.5851	6.0209	0.3970	1.4537	0.0418	0.2597
1119	0.0	0.5444	6.1598	0.4349	1.5503	0.0207	0.1272
1120	0.0	0.5455	5.6364	0.3518	1.4625	0.0356	0.0909
1121	0.0	0.4775	6.8201	0.4118	1.3737	0.0346	0.0519
1122	0.0035	0.6000	6.6807	0.3088	1.6140	0.0175	0.0947
1123	0.0165	0.5842	5.9274	0.5347	1.5149	0.0594	0.0825
1124	0.0258	0.4710	6.7839	0.3710	1.4484	0.0516	0.1065
1125	0.0211	0.4070	6.1404	0.2281	1.5053	0.0316	0.0561
1126	0.0152	0.5361	5.4525	0.3992	1.3916	0.0380	0.0494
1127	0.0136	0.7449	6.1837	0.3707	1.4218	0.0374	0.0612
1128	0.0191	0.4675	6.1183	0.3969	1.2328	0.0	0.0420
1129	0.0299	0.5821	6.1828	0.5224	1.7724	0.0373	0.0672
1130	0.0385	0.6399	5.4650	0.2517	1.5559	0.0350	0.2238
1131	0.0214	0.6477	7.0071	0.5801	1.7295	0.0605	0.1246
1132	0.0247	0.5512	5.4046	0.3246	1.2191	0.0459	0.1519
1133	0.0217	0.0939	6.5235	0.4332	1.4404	0.0361	0.1372
N	25	28	28	28	28	27	28
MEAN	0.0172	0.5725	6.2196	0.4118	1.4975	0.0367	0.1013
S.D.	0.0077	0.1390	0.4316	0.0999	0.1389	0.0098	0.0537
S.E.	0.0015	0.0263	0.0816	0.0189	0.0262	0.0019	0.0101

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 2 - 210 ppm

DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
1169	0.0274	0.6062	6.0685	0.3664	1.4692	0.0342	0.1336
1170	0.0188	0.6928	5.9812	0.3542	1.6364	0.0313	0.1034
1171	0.0098	0.6885	6.5475	0.3410	1.5639	0.0328	0.0787
1172	0.0137	0.5256	4.4983	0.1775	1.1980	0.0	0.0785
1173	0.0200	0.5333	6.1533	0.2600	1.3600	0.0300	0.0633
1174	0.0178	0.4520	5.2384	0.6014	1.4199	0.0427	0.2349
1175	0.0115	0.5038	5.0344	0.4160	1.8244	0.0382	0.0802
1176	0.0185	0.8450	6.3505	0.2952	1.5609	0.0369	0.1882
1177	0.0099	0.5493	6.7105	0.3191	1.5132	0.0395	0.1151
1178	0.0179	0.7276	5.4588	0.3907	1.6667	0.0251	0.1147
1179	0.0121	0.4113	4.8589	0.4919	1.3831	0.0202	0.0968
1180	0.0215	0.4910	6.1685	0.3835	1.6165	0.0215	0.1613
1181	0.0207	0.4345	6.6172	0.4379	1.4517	0.0310	0.1172
1182	0.0286	0.4464	6.5571	0.4643	1.7071	0.0286	0.0821
1183	0.0227	0.5000	6.4886	0.4811	1.3939	0.0	0.1326
1184	0.0294	0.6267	6.0221	0.5110	1.5000	0.0368	0.1176
1186	0.0185	1.3415	7.3323	1.0677	2.1138	0.0308	0.7908
1187	0.0160	0.6837	5.6294	0.3419	1.3802	0.0256	0.0447
1188	0.0	1.7370	7.2741	1.1074	2.3000	0.0185	0.9444
1189	0.0	0.4983	4.9308	0.3910	1.2664	0.0277	0.1696
1190	0.0	0.5849	6.6321	0.5566	1.5660	0.0220	0.1289
1191	0.0174	0.6354	7.4201	0.3715	1.7812	0.0278	0.2708
1192	0.0070	0.4913	6.2369	0.1951	1.3728	0.0	0.1254
1194	0.0129	0.8006	6.2058	0.4437	1.6431	0.0	0.1415
1195	0.0094	0.7170	6.5409	0.4088	1.5314	0.0252	0.1761
1196	0.0143	0.7479	5.8214	0.3786	1.5464	0.0250	0.1250
1197	0.0093	0.7864	7.2136	0.3932	1.7864	0.0217	0.0650
1198	0.0300	0.6652	5.4506	0.2060	1.4206	0.0343	0.1373
N	25	28	28	28	28	24	28
MEAN	0.0174	0.6695	6.1586	0.4340	1.5705	0.0295	0.1792
S.D.	0.0066	0.2792	0.7728	0.2101	0.2372	0.0066	0.2018
S.E.	0.0013	0.0528	0.1460	0.0397	0.0448	0.0013	0.0381

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 3 - 700 ppm

DIMP

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1233	0.0285	0.5696	5.9494	0.3766	1.4715	0.0348	0.0380
1234	0.0122	0.5335	6.3354	0.2896	1.4482	0.0305	0.0762
1235	0.0140	0.6611	6.7703	0.3361	1.5350	0.0224	0.0784
1236	0.0251	0.7455	6.3190	0.3405	1.6021	0.0394	0.0466
1237	0.0215	0.6523	4.2115	0.5018	1.4014	0.0	0.0358
1238	0.0099	0.5530	4.7649	0.4901	1.3113	0.0298	0.1987
1239	0.0	0.7349	6.0422	0.4428	1.6235	0.0271	0.1355
1240	0.0089	0.5952	5.6399	0.2232	1.5714	0.0268	0.1310
1241	0.0130	0.7500	5.2695	0.4773	1.5617	0.0	0.1331
1242	0.0146	0.6606	5.1788	0.2518	1.6496	0.0292	0.0949
1243	0.0069	0.5379	5.9241	0.3069	1.4241	0.0345	0.0724
1244	0.0076	0.5758	7.0379	0.4053	1.5795	0.0417	0.0303
1245	0.0065	0.7026	7.0654	0.4281	1.5654	0.0	0.0392
1246	0.0191	0.6374	6.4809	0.4924	1.5725	0.0534	0.0496
1247	0.0243	0.7396	7.1111	0.3993	1.6285	0.0382	0.1076
1248	0.0073	0.4270	6.1460	0.3759	1.4051	0.0219	0.0036
1249	0.0095	0.5079	6.4381	0.3556	1.4603	0.0286	0.0794
1250	0.0160	0.6326	6.7540	0.3994	1.8371	0.0351	0.0927
1251	0.0132	0.6337	6.3564	0.3861	1.5215	0.0627	0.1353
1252	0.0139	0.6528	7.0139	0.4556	1.5972	0.0306	0.1639
1253	0.0185	0.6400	5.7231	0.4831	1.4831	0.0277	0.1046
1254	0.0131	0.7549	6.3248	0.2974	1.5131	0.0	0.0948
1255	0.0146	0.5766	5.5328	0.3832	1.4307	0.0328	0.1277
1256	0.0064	0.6975	6.6497	0.4395	1.6465	0.0255	0.1465
1257	0.0232	0.8108	5.2317	0.3205	1.4517	0.0425	0.2008
1258	0.0138	0.5345	5.4552	0.2724	1.4897	0.0310	0.0586
1259	0.0	0.8062	7.3149	0.5363	1.6678	0.0554	0.0761
1260	0.0106	0.6007	6.3887	0.4523	1.5124	0.0247	0.1413
1261	0.0201	0.5582	6.1606	0.3695	1.5984	0.0321	0.0402
1262	0.0158	0.6008	5.8617	0.6601	1.5455	0.0435	0.0514
N	28	30	30	30	30	26	30
MEAN	0.0146	0.6361	6.1151	0.3983	1.5369	0.0347	0.0928
S.O.	0.0061	0.0925	0.7366	0.0938	0.1030	0.0102	0.0503
S.E.	0.0011	0.0169	0.1345	0.0171	0.0188	0.0020	0.0092

TABLE I-E-14 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 4 - 2100 ppm

DIMP

ANIMAL NUMMER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
1297	0.0117	0.5702	6.7895	0.3713	1.4240	0.0205	0.1930
1298	0.0163	0.4739	5.6503	0.3758	1.4444	0.0392	0.1307
1299	0.0172	0.5905	5.9612	0.3147	1.5948	0.0345	0.0690
1300	0.0328	0.5475	7.0295	0.6426	1.8820	0.0623	0.2328
1301	0.0269	0.6566	6.4916	0.3771	1.5993	0.0337	0.1616
1302	0.0068	0.5666	5.6724	0.3072	1.6451	0.0137	0.0887
1303	0.0067	0.4732	5.5101	0.3960	1.7383	0.0336	0.0436
1304	0.0065	0.4742	5.4774	0.5677	1.4516	0.0194	0.1742
1305	0.0092	0.5446	5.4800	0.3077	1.3415	0.0308	0.0585
1306	0.0	0.5200	4.4277	0.3231	1.1477	0.0308	0.1231
1307	0.0157	0.3041	6.3166	0.2414	1.5329	0.0282	0.1567
1308	0.0114	0.4943	5.2167	0.4144	1.4183	0.0380	0.1065
1309	0.0121	0.5081	6.2782	0.4153	1.6573	0.0323	0.1613
1310	0.0033	0.3813	5.2241	0.4247	1.1973	0.0	0.1739
1311	0.0102	0.6054	6.4422	0.4592	1.8197	0.0374	0.1565
1312	0.0111	0.6310	6.1365	0.3432	1.3063	0.0	0.0664
1313	0.0169	0.8068	7.2475	0.4983	1.6814	0.0373	0.0475
1314	0.0108	0.7690	6.7762	0.4765	1.8051	0.0397	0.1119
1315	0.0172	0.5276	6.8897	0.5207	1.7138	0.0	0.1069
1316	0.0129	0.7065	5.9290	0.3516	1.5677	0.0323	0.0839
1317	0.0306	0.4660	5.1020	0.3639	1.2789	0.0340	0.0748
1318	0.0418	0.7944	7.9721	0.3902	1.7700	0.0314	0.0418
1319	0.0611	0.8000	6.5556	0.4667	1.3944	0.0556	0.0
1320	0.0333	0.7593	7.2667	0.3444	1.6704	0.0407	0.0852
1321	0.0255	0.6473	5.1455	0.3782	1.4109	0.0364	0.0473
1322	0.0115	0.9504	6.2328	0.4962	1.9542	0.0687	0.0687
1323	0.0177	0.5936	7.0495	0.5194	1.6643	0.0353	0.2049
1324	0.0194	0.8129	5.9806	0.3871	1.6355	0.0290	0.1226
1325	0.0110	0.6287	6.4118	0.5478	1.7279	0.0294	0.2169
1326	0.0138	0.5103	7.4655	0.4345	1.6000	0.0379	0.1241
N	29	30	30	30	30	27	29
MEAN	0.0180	0.6038	6.2043	0.4152	1.5692	0.0356	0.1184
S.D.	0.0124	0.1449	0.8207	0.0898	0.2020	0.0116	0.0558
S.E.	0.0023	0.0265	0.1498	0.0164	0.0369	0.0022	0.0104

AD-A058 323

LITTON BIONETICS INC KENSINGTON MD  
MAMMALIAN TOXICOLOGICAL EVALUATION OF DIMP AND DCPD.(U)  
NOV 76 E R HART

F/G 6/20

DAMD17-75-C-5068

NL

UNCLASSIFIED

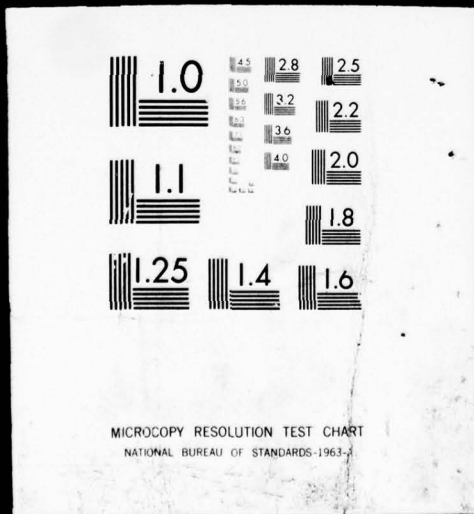
2 of 3  
AD  
A068323



# SIFTED

## 2 OF 3

### AD A058323



KEY FOR INCIDENCE TABLES

- + = Present
- 1 = Minimal
- 2 = Mild
- 3 = Moderate
- 4 = Marked
- o = Tissue Missing
- N/A = Nonapplicable
- = Negative

TABLE I-E-15

## 90-DAY TOXICITY STUDY IN MICE

## DIMP

## INCIDENCE OF HISTOLOGIC FINDINGS

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
Animal No.	1084	1089	1091	1096	1098	1118	1123	1124	1129	1130	1285	1288	1289	1291	1292	1317	1318	1319	1320	1321
Tissue Findings																				
Thyroid	-	0	0	0	0	-	-	-	-	0	0	-	-	-	0	-	-	-	-	0
Lung*																				
Bronchioalveolar adenomas				+																
Bronchitis																				
Chronic murine pneumonia																				
Heart																				
Mesenteric Lymph Node				0					0	0	0	-	-	-	-	-	-	-	-	0
Liver																				
Focal hemosiderosis						+														
Chronic periportal hepatitis																				
Spleen																				
Pancreas																				
Stomach																				
Small Intestine																				
Large Intestine																				
Nematodiasis	+	+			+	+			+		+	+	+	+	+	+	+	+	+	+
Kidneys																				
Adrenal Glands	0					0				0										

\* Microscopic examination made only when gross lesions found.

TABLE I-E-15 (Continued)

## 90-DAY TOXICITY STUDY IN MICE

## DIMP

## INCIDENCE OF HISTOLOGIC FINDINGS (Continued)

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
Animal No.	1084	1089	1091	1096	1098	1118	1123	1124	1129	1130	1285	1288	1289	1291	1292	1317	1318	1319	1320	1321
Tissue Findings	-	-	-	-	-	-	-	-	-	-	0	-	0	-	-	-	0	-	-	-
Urinary Bladder	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Testes with Epididymis	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	0	-	-	-
Ovaries	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	0	-	-	-
Uterus	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Prostate	-	-	-	0	-	N/A	N/A	N/A	N/A	N/A	0	-	0	-	0	N/A	N/A	N/A	N/A	N/A
Seminal Vesicles	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eyes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

PART I - SECTION F  
14-DAY TOXICITY STUDY IN DOGS

DIMP

LBI PROJECT NO. 2565

SUMMARY

Feeding of DIMP to male and female dogs for 14 days at 150, 500, and 1500 ppm did not lead to development of evidence of toxicity.

1. OBJECTIVE

The purpose of this study was to characterize the subacute toxicity of DIMP in dogs.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in beagle dogs obtained from Hazleton Research Animals, Cumberland, Virginia, with body weights averaging 11.1 kg for males and 9.5 kg for females at initiation.

B. Animal Groups

The dogs were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	1	1	Zero - Control
2	1	1	Low - 150 ppm
3	1	1	Medium - 500 ppm
4	1	1	High - 1500 ppm

C. Diet Preparation

The dogs were fed Purina Dog Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

3. EXPERIMENTAL DESIGN (continued)

D. Observations

Body weights and food consumption were recorded weekly. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects.

E. Clinical Laboratory Measurements

The following determinations were made on all dogs initially and again just before termination:

Hematology

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	

Clinical Biochemistry

blood sugar	SGPT
blood urea nitrogen (BUN)	SGOT
total protein	alkaline phosphatase
total bilirubin	

Urinalysis

pH	ketones
specific gravity	total protein
glucose	

F. Termination and Postmortem Examination

Upon conclusion of the study, the animals were killed and subjected to careful gross necropsy under the supervision of a veterinary pathologist. The following organs were removed and weighed individually:

thyroid	spleen	testes with epididymis
heart	kidneys	ovaries
liver	adrenals	

### 3. EXPERIMENTAL DESIGN (continued)

#### F. Termination and Postmortem Examination

Samples of the following tissues were taken for preservation in 10% neutral formalin:

mammary gland	stomach	uterus
thyroid	small intestine	bone marrow
lung	large intestine	brain
heart	kidneys	pituitary
liver	adrenals	thoracic spinal cord
gall bladder	urinary bladder	eye
spleen	testes	nerve with muscle
pancreas	ovary	rib junction
mesenteric lymph node	prostate	any unusual lesions

The following tissues from each animal in the control and the high dosage groups were prepared and examined for histopathologic alteration:

thyroid	spleen	adrenals
lung	stomach	bone marrow
heart	small intestine	brain
liver	kidney	lesions

### 4. RESULTS

All dogs survived the period of the study without incidence of adverse effect.

All clinical laboratory determinations resulted in values within the limits of normal.

Body weights fluctuated somewhat as is felt to be normal for adult dogs. Food consumption also varied in a normal way.

Terminal sacrifice and all aspects of the postmortem examination were conducted under the supervision of Herman R. Seibold, V.M.D., of Bionetics' Pathology Department. These tabulations of organ weights and gross and microscopic postmortem findings and a signed summary are attached. He reports no noteworthy deviations.

### 5. CONCLUSIONS

Feeding of DIMP to male and female dogs for 14 days at 150, 500, and 1500 ppm did not lead to development of evidence of toxicity.

14-DAY TOXICITY STUDY IN DOGS

DIMP

LBI PROJECT NO. 2565

Summary of the Gross and Histological Examination of Tissue

Tissues from the control and high dose experimental animals were examined microscopically. Tissues, animal identification, drug identification and dose are listed in tables on (1) Necropsy Observations and (2) Histological findings.

Repeated abnormality was found only in mesenteric lymph nodes and was recognized in the gross, as reddening of the medullary area (on section of the node) and microscopically, as hemorrhage and erythrophagocytosis. The incidence of the hemorrhage and erythrophagocytosis, among principals versus controls did not indicate a relation with the treatments. The mesenteric nodes had not been specified (in the protocol) for microscopic examination, consequently only the nodes with gross abnormalities were examined microscopically.

In no instance did an organ or tissue specified for microscopic examination present a noteworthy difference in microscopic appearance from corresponding organs or tissues of the dogs in the same group or in different groups.

March 25, 1976  
Date

H. R. Seibold  
Herman R. Seibold, V.M.D.  
Pathologist

TABLE I-F-16

BODY WEIGHTS  
(Kilograms)

DIMP

<u>DOG NO.</u>	<u>SEX</u>	<u>INTERVAL</u>		
		<u>WK 0</u>	<u>WK 1</u>	<u>WK 2</u>
<u>GROUP 1 - CONTROL</u>				
265	M	10.4	11.0	11.0
252	F	8.8	10.1	9.3
<u>GROUP 2 - 150 ppm</u>				
267	M	10.8	11.4	10.8
259	F	9.6	9.6	9.1
<u>GROUP 3 - 500 ppm</u>				
264	M	11.2	12.3	12.3
257	F	9.8	11.0	10.1
<u>GROUP 4 - 1500 ppm</u>				
263	M	11.8	12.7	12.3
253	F	9.6	10.4	10.4

TABLE 1-F-17  
FOOD CONSUMPTION  
(Kilograms)

DIMP

<u>DOG NO.</u>	<u>SEX</u>	<u>INTERVAL</u>		
		<u>WK 1</u>	<u>WK 2</u>	<u>WK 3</u>
<u>GROUP 1 - CONTROL</u>				
265	M	2.6	1.8	2.2
252	F	2.0	2.1	1.7
<u>GROUP 2 - 150 ppm</u>				
267	M	1.8	1.5	1.5
259	F	2.0	1.7	1.8
<u>GROUP 3 - 500 ppm</u>				
264	M	2.6	2.1	3.0
257	F	1.8	1.5	1.7
<u>GROUP 4 - 1500 ppm</u>				
263	M	2.3	2.2	2.0
253	F	2.6	2.2	1.8

TABLE I-F-18

## HEMATOCYTOLOGY

PRE-DRUG - DIMP

DOG NO.	SEX	CELL VOL. %	HEMO-GLOBIN gm %	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*								
						My	Juv	Ban	Seg	Ly	Mo	Eo	Bas	AtL
GROUP 1 - CONTROL														
265	M	49.0	16.4	7.52	14.7	0	0	0	0	67	28	1	4	0
252	F	48.5	16.1	7.73	15.5	0	0	0	0	53	44	0	3	0
GROUP 2 - 150 ppm														
267	M	44.0	14.4	6.40	8.3	0	0	0	0	61	37	1	1	4
259	F	49.0	16.8	7.90	7.9	0	0	0	0	63	36	0	1	2
GROUP 3 - 500 ppm														
264	M	43.5	14.1	6.79	16.4	0	0	0	0	78	21	0	1	1
257	F	48.0	16.6	8.13	11.2	0	0	0	0	44	55	0	1	0
GROUP 4 - 1500 ppm														
263	M	46.0	15.9	7.00	11.8	0	0	0	0	53	43	1	4	2
253	F	46.0	15.7	8.16	14.4	0	0	0	0	64	34	1	1	1

\* Differential (%) - My = Myelocytes; Juv = Juveniles; Ban = Bands; Seg = Segmented Neutrophils; Ly = Lymphocytes; Mo = Monocytes; Eo = Eosinophils; Bas = Basophils; AtL = Atypical Lymphocytes.

TABLE I-F-18 (Continued)

## HEMATOCYTOLOGY

## TERMINAL - DIMP

DOG NO.	SEX	CELL VOL. %	HEMO- GLOBIN gm %	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*									
						My	Juv	Ban	Seg	Ly	Mo	Eo	Bas	AtL	
GROUP 1 - CONTROL															
265	M	50.0	17.0	7.05	9.6	0	0	0	0	51	44	1	4	0	0
252	F	49.0	16.3	6.66	9.9	0	0	0	0	52	42	6	0	0	0
GROUP 2 - 150 ppm															
267	M	43.0	14.3	6.25	8.0	0	0	0	0	50	46	2	2	0	0
259	F	48.5	16.7	6.78	9.3	0	0	0	0	46	52	0	2	0	0
GROUP 3 - 500 ppm															
264	M	47.5	15.3	6.66	11.0	0	0	0	0	64	30	3	3	0	0
257	F	46.0	15.0	7.11	7.3	0	0	0	0	68	27	3	2	0	0
GROUP 4 - 1500 ppm															
263	M	45.5	15.2	6.36	11.2	0	0	0	0	45	52	1	2	0	0
253	F	45.0	15.2	6.65	10.2	0	0	0	0	54	43	2	1	0	0

\* Differential (%) - My = Myelocytes; Juv = Juveniles; Ban = Bands; Seg = Segmented Neutrophils; Ly = Lymphocytes;  
Mo = Monocytes; Eo = Eosinophils; Bas = Basophils; AtL = Atypical Lymphocytes.

TABLE I-F-19

BLOOD CHEMISTRY  
PRE-DRUG - DIMP

DOG NO.	SEX	BUN mg %	GLU- COSE mg %	ALK. PHOS. I.U.	SGOT I.U.	T. BILI- RUBIN mg %	TOTAL PROTEIN gm %	SGPT I.U.
<u>GROUP 1 - CONTROL</u>								
265	M	13	96	87	39	0.3	6.0	29
252	F	14	116	73	30	0.3	6.2	32
<u>GROUP 2 - 150 ppm</u>								
267	M	9	114	49	24	0.3	6.2	34
259	F	13	117	110	44	0.3	6.2	34
<u>GROUP 3 - 500 ppm</u>								
264	M	13	88	105	48	0.3	6.5	39
257	F	11	111	84	26	0.3	5.5	24
<u>GROUP 4 - 1500 ppm</u>								
263	M	13	94	90	37	0.4	6.3	38
253	F	14	93	103	42	0.4	6.2	32

TABLE I-F-19 (Continued)

## BLOOD CHEMISTRY

## TERMINAL - DIMP

DOG NO.	SEX	BUN mg %	GLU- COSE mg %	ALK. PHOS. I.U.	SGOT I.U.	LDH I.U.	T.BILI- RUBIN mg %	Ca mg %	PHOS- PHORUS mg %	CREAT- ININE mg %	URIC ACID mg %	CHOLE- STEROL mg %	TOTAL PROTEIN gm %	AL- BUMIN gm %	SGPT I.U.
GROUP 1 - CONTROL															
265	M	14	104	86	27	212	0.2	10.4	5.2	0.8	0.4	122	6.0	3.5	32
252	F	14	155	69	36	173	0.1	10.7	4.6	0.9	0.4	169	6.2	3.7	46
GROUP 2 - 150 ppm															
267	M	10	106	49	31	83	0.1	10.8	5.9	0.7	0.3	138	5.6	3.5	43
259	F	9	114	113	35	221	0.2	10.1	4.2	0.8	0.4	141	6.2	3.7	38
GROUP 3 - 500 ppm															
264	M	15	102	93	33	175	0.2	10.5	6.1	0.7	0.4	172	6.5	3.8	48
257	F	11	99	83	26	182	0.3	10.2	5.5	0.8	0.4	114	5.7	3.3	35
GROUP 4 - 1500 ppm															
263	M	12	103	105	27	126	0.2	10.8	6.2	0.8	0.3	159	5.9	3.4	45
253	F	21	100	87	32	204	0.1	11.0	5.1	1.0	0.4	215	6.3	3.6	38

## URINALYSIS

### KEY

Color: Y = Yellow  
Or = Orange  
Br = Brown  
Str = Straw

Casts: fgr = Finely Granular

Crystals: T.P. = Triple Phosphate  
U.A. = Uric Acid  
Ca O = Calcium Oxalate

- or 0 = None or Negative  
+ = Trace, Occasional, Rare,  
- Very Little  
1+ = Slight, Small, Little,  
Few, Some, Light  
2+ = Moderate, Frequent, Large  
3+ = Severe, Heavy, Many  
4+ = Maximal  
TNTC = Too Numerous to Count

TABLE I-F-20

## URINALYSIS

PRE-DRUG - DIMP

DOG NO.	SEX	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	BILIRUBIN	OCULT BLOOD	MBC	MICROSCOPIC EXAMINATION/HPF*							
												RBC	EPITH	CASTS	AMORPH	BACT	CRYSTALS		
																	U.A.	Y.P.	
GROUP 1 - CONTROL																			
265	M	Y	Cloudy	1.017	6	0	0	0	0	0	4-5	-	3-4	-	-	-	-		
252	F	Y	Cloudy	1.024	7	0	0	0	0	0	5-6	3-4	1-2	-	±	-	-		
GROUP 2 - 150 ppm																			
267	M	Y	Cloudy	1.015	7	0	0	0	0	0	3-4	-	1-2	-	2+	-	-		
259	F	Y	Cloudy	1.020	7	0	0	0	0	0	4-5	-	1-2	-	3+	-	-		
Group 3 - 500 ppm																			
264	M	Y	Cloudy	1.023	6	0	0	0	0	0	3-4	-	-	-	1+	-	-		
257	F	Y	Cloudy	1.024	7	0	0	0	0	0	1-2	0-1	1-2	-	-	-	-		
Group 4 - 1500 ppm																			
263	M	Y	Cloudy	1.027	7	0	0	0	0	0	1-2	-	-	-	1+	-	1-2		
253	F	Y	Cloudy	1.021	7	0	0	0	0	0	8-9	-	-	0-1fgr	1+	-	1+		

\*Microscopic examination per high power field.

TABLE I-F-20 (Continued)

URINALYSIS																		
TERMINAL - DIMP																		
DOG NO.	SEX	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLU-COSE	KE-TONES	BILLI-RUBIN	OCCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*							
											CRYSTALS							OTHER
											U.A.	T.P.	BACT	AMORPH	CASTS	EPITH	RBC	
265	M	Y	Cloudy	1.033	6	0	0	0	0	0	0-1	1-2	-	-	1+	-	-	-
252	F	Y	Clear	1.018	5	0	0	0	0	0	0-1	1-2	-	-	-	-	-	-
267	M	Y	Cloudy	1.020	6	0	0	0	0	0	-	2-3	-	-	1+	-	±	-
259	F	Y	Cloudy	1.005	5	0	0	0	0	0	1-2	-	-	-	3+	-	-	-
264	M	Y	Cloudy	1.026	6	0	0	0	0	0	2-3	3-4	-	-	-	-	-	-
257	F	Y	Cloudy	1.028	8	0	0	0	0	0	-	-	-	-	1+	-	-	-
263	M	Y	Cloudy	1.028	6	0	0	0	0	0	-	2-3	-	-	-	±	-	-
253	F	Y	Cloudy	1.029	6	0	0	0	0	0	2-3	4-5	-	-	1+	-	-	-

\*Microscopic examination per high power field.

TABLE I-F-21

## 14-DAY TOXICITY STUDY IN DOGS

## HISTOLOGICAL FINDINGS

## DIMP

GROUP	1-CONTROL		4-1500 PPM	
SEX	M	F	M	F
DOG NUMBER	265	252	263	253
PATHOLOGY NUMBER (76-1__)	478	479	484	485

Tissue/Findings

Thyroid	-	-	-	-
Lung	-	-	-	-
Heart	-	-	-	-
Liver	-	-	-	-
Spleen	-	-	-	-
Mesenteric Lymph Nodes				
Hemorrhage	3		3	
Erythrophagocytosis	3		3	
Stomach	-	-	-	-
Small Intestine	-	-	-	-
Large Intestine	-	-	-	-
Kidneys	-	-	-	-
Adrenals	-	-	-	-
Bone Marrow	-	-	-	-
Brain	-	-	-	-

## LEGEND FOR TABLE

- = tissue within normal histological limits  
 3 = moderate

TABLE I-F-22

## 14-DAY TOXICITY STUDY IN DOGS

## NECROPSY OBSERVATIONS

## DIMP

GROUP	1-CONTROL		2-150 PPM		3-500 PPM		4-1500 PPM	
SEX	M	F	M	F	M	F	M	F
DOG NUMBER	265	252	267	259	264	257	263	253
PATHOLOGY NO. (76-1___)	478	479	480	481	482	483	484	485

Tissue/Findings

Thyroid	-	-	-	-	-	-	-	-
Lung	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-
Gall bladder								
Granular mucosa	-	-	-	3	-	-	-	-
Spleen	-	-	-	-	-	-	-	-
Mesenteric Lymph Nodes								
Reddening of medullary area	3	-	3	-	-	-	3	-
Stomach	-	-	-	-	-	-	-	-
Small Intestine	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	-	-	-	-
Kidneys	-	-	-	-	-	-	-	-
Adrenals	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-

## LEGEND FOR TABLE

- = gross abnormalities not observed  
3 = moderate

TABLE I-F-23

## 14-DAY TOXICITY STUDY IN DOGS

## ORGAN WEIGHTS

## DIMP

<u>DOG NO.</u>	<u>SEX</u>	<u>THYROID</u>	<u>HEART</u>	<u>LIVER</u>	<u>SPLEEN</u>	<u>KIDNEYS</u>	<u>ADRENALS</u>	<u>GONADS</u>
				<u>GROUP 1 - CONTROL</u>				
265	M	1.00	80.60	325.60	94.46	27.38(rt.) 28.63(lt.)	0.50(rt.) 0.43(lt.)	6.80(rt.) 6.91(lt.)
252	F	1.21	72.78	315.97	51.60	24.82(rt.) 25.09(lt.)	0.53(rt.) 0.48(lt.)	0.35(rt.) 0.29(lt.)
				<u>GROUP 2 - 150 PPM</u>				
267	M	0.96	96.06	319.90	135.16	32.33(rt.) 32.91(lt.)	0.53(rt.) 0.44(lt.)	7.69(rt.) 8.20(lt.)
259	F	0.92	65.17	266.80	62.96	24.50(rt.) 25.66(lt.)	0.44(rt.) 0.49(lt.)	0.43(rt.) 0.35(lt.)
				<u>GROUP 3 - 500 PPM</u>				
264	M	0.87	82.42	362.69	83.62	35.47(rt.) 36.42(lt.)	0.50(rt.) 0.21(lt.)	7.40(rt.) 7.49(lt.)
257	F	-	83.05	257.70	54.64	26.84(rt.) 26.92(lt.)	0.47(rt.) 0.46(lt.)	0.38(rt.) 0.41(lt.)
				<u>GROUP 4 - 1500 PPM</u>				
263	M	0.93	80.69	391.01	42.57	32.48(rt.) 33.78(lt.)	0.54(rt.) 0.57(lt.)	10.31(rt.) 11.47(lt.)
253	F	1.20	65.62	308.76	60.57	21.69(rt.) 22.88(lt.)	0.48(rt.) 0.39(lt.)	0.34(rt.) 0.37(lt.)

PART I - SECTION G  
PRIMARY EYE IRRITATION STUDY IN RABBITS

DIMP

LBI PROJECT NO. 2560

SUMMARY

The Draize Eye Irritation Test revealed significant signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Some irritation occurred in spite of irrigation two or four seconds after the application, but only in the absence of irrigation was its degree important. In all but one case the irritation had cleared by the seventh day postexposure. That one was clear on Day 8.

1. OBJECTIVE

The objective of this study was to investigate the possibility that direct contamination of the eye with the test material would be followed by irritation and/or injury.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Eye irritancy was studied by direct application of the liquid material to the conjunctival sac of one eye of an albino rabbit of the New Zealand White strain. The procedure is widely known as the Draize Eye Irritation Test.

Nine rabbits were used for this study. The chosen eye (usually left) of each rabbit was stained with fluorescein and examined with the aid of magnification and fluorescent lighting to ascertain that it was clear of any lesions before application of the test material. With an assistant holding the animal and forming a pouch of the lower eyelid, a sample of 0.1 ml of the material was delivered directly into the conjunctival sac. After delivery of the material, the eyelid was released and the lids gently pressed together momentarily. Following this, the treated eyes of three animals were washed with about 20 ml of lukewarm water two seconds after application; the eyes of three more animals were washed at four seconds; and the remainder were not washed. The opposite eye remained untreated and served as a control.

3. EXPERIMENTAL DESIGN (continued)

After the initial application, each eye was examined at least daily for 7 days and again at 14 days. Observations were carried out by experienced observers and a copy of the "Illustrated Guide for Grading Eye Irritation By Hazardous Substances" was at hand during the conduct of this experiment. The scale used for scoring ocular lesions is attached.

4. RESULTS

A complete tabulation of the scores recorded for each of the nine animals used is presented in Table I-G-24. The results may be summarized by a statement that significant irritation of the conjunctivae was observed in all nine animals at one day following application of the test material. Irritation was reduced but not prevented by irrigation two or four seconds after application. In the absence of irrigation there was diffuse opacity of most of the corneal surface. In all cases the eyes were normal by the eighth day.

5. CONCLUSIONS

The Draize Eye Irritation Test revealed significant signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Some irritation occurred in spite of irrigation two or four seconds after the application, but only in the absence of irrigation was its degree important. In all but one case the irritation had cleared by the seventh day postexposure. That one was clear on Day 8.

TABLE I-G-24

## EYE IRRITATION SCORES - RABBITS

DIMP

		NOT IRRIGATED													
		6154							6147						
ANIMAL	OBS. TIME (DAYS)	1	2	3	4	7	14		1	2	3	4	5	6	7
Cornea		0	0	0	0	0	0		4	4	4	4	4	4	0
Iris		0	0	0	0	0	0		0	0	0	0	0	0	0
Conjunctivae		1	1	0	0	0	0		2	2	3	3	2	1	0
Total Score		2	2	0	0	0	0		24	24	26	26	24	22	0
									4	24	4	2	2	2	0

		IRRIGATED AT 2 SECONDS													
		6161							6150						
ANIMAL	OBS. TIME (DAYS)	1	2	3	4	7	14		1	2	3	4	7	14	
Cornea		0	0	0	0	0	0		0	0	0	0	0	0	0
Iris		0	0	0	0	0	0		0	0	0	0	0	0	0
Conjunctivae		1	0	0	0	0	0		1	2	1	0	0	0	0
Total Score		2	0	0	0	0	0		2	4	2	0	0	0	0

		IRRIGATED AT 4 SECONDS													
		6172							6152						
ANIMAL	OBS. TIME (DAYS)	1	2	3	4	7	14		1	2	3	4	5	6	7
Cornea		0	0	0	0	0	0		0	0	0	0	0	0	0
Iris		0	0	0	0	0	0		0	0	0	0	0	0	0
Conjunctivae		1	1	0	0	0	0		1	2	2	2	1	0	0
Total Score		2	2	0	0	0	0		2	4	4	4	2	0	0
									2	2	0	0	0	0	0

# SCALE FOR SCORING OCULAR LESIONS\*

## (1) CORNEA

- (A) Opacity-degree of density (area most dense taken for reading)
- No Opacity . . . . . 0
  - Scattered or diffuse area, details of iris clearly visible . . . . 1
  - Easily discernible translucent areas, details of iris slightly obscured . . . . . 2
  - Opalescent areas, no details of iris visible, size of pupil barely discernible . . . . . 3
  - Opaque, iris invisible . . . . . 4
- (B) Area of cornea involved
- One quarter (or less) but not zero . . . . . 1
  - Greater than one quarter, but less than half . . . . . 2
  - Greater than half, but less than three quarters . . . . . 3
  - Greater than three quarters, up to whole area . . . . . 4
- Score equals A x B x 5 Total maximum = 80

## (2) IRIS

- (A) Values
- Normal . . . . . 0
  - Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reactions is positive) . . . . . 1
  - No reaction to light, hemorrhage, gross destruction (any or all of these) . . . . . 2
- Score equals A x 5 Total maximum = 10

## (3) CONJUNCTIVAE

- (A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)
- Vessels normal . . . . . 0
  - Vessels definitely injected above normal . . . . . 1
  - More diffuse, deeper crimson red, individual vessels not easily discernible . . . . . 2
  - Diffuse beefy red . . . . . 3
- (B) Chemosis
- No swelling . . . . . 0
  - Any swelling above normal (includes nictitating membrane) . . . . 1
  - Obvious swelling with partial eversion of lids . . . . . 2
  - Swelling with lids about half closed . . . . . 3
  - Swelling with lids about half closed to completely closed . . . . 4
- (C) Discharge
- No discharge . . . . . 0
  - Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) . . . . . 1
  - Discharge with moistening of the lids and hairs just adjacent to lids . . . . . 2
  - Discharge with moistening of the lids and hairs, and considerable area around the eye . . . . . 3
- Score equals (A + B + C) x 2 Total maximum = 20

The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctivae. Total maximum score possible = 110

\*Lehman, A. J., et al., Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Assoc. Food and Drug Officials of the U. S., Austin, Texas, 1959.

PART I - SECTION H  
ACUTE DERMAL IRRITATION STUDY IN RABBITS

DIMP

LBI PROJECT NO. 2561

SUMMARY

Application of DIMP to the intact and abraded skin at doses of 0.2, 0.63, and 2.0 g/kg produced only minimal skin irritation. Death occurred in 3/4 at the highest dosage and in 1/4 at the intermediate dosage.

1. OBJECTIVE

The purpose of this study was to evaluate the toxicity of DIMP following a single application to the skin of rabbits. The design of the study afforded an insight into the systemic toxicity as well as an evaluation of the potential for skin irritation.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Twelve male New Zealand White (albino) rabbits, obtained from B and H Rabbitry, Rockville, Maryland, were acclimated to laboratory conditions for at least two weeks. Single graded doses (0.2, 0.63, and 2.0 g per kilogram of body weight) of the undiluted test substance, DIMP, were administered by dermal application to groups consisting of four male rabbits each. The hair was clipped closely on the backs of all rabbits prior to application. The skin of two rabbits per dose group was abraded by making minor incisions through the stratum corneum. These incisions were not sufficient to disturb the derma and bleeding was not produced. After application of the test material to the prepared skin of the back, the area treated was covered with cotton gauze and the trunk was covered with rubber dental damming. A flange-type collar was fitted in order to limit the rabbit's access to the application.

During the acclimation period and throughout the study, the rabbits were individually housed in wire-bottom cages in temperature-controlled quarters under artificial lighting automated to provide a 12-hour light to dark cycle in each day. Purina Rabbit Chow and water were provided ad libitum.

### 3. EXPERIMENTAL DESIGN (Continued)

The rabbits were observed for mortality and other signs of intoxication on the day of application and daily thereafter for 14 days. Body weights were recorded initially and at the termination of the study. The collar and covering over the area of application were removed after 24 hours and the excess test material removed. The effect on the skin was evaluated at that time and daily thereafter until the termination of the study according to the scoring system described in the Federal Hazardous Substances Act as follows:

<u>Erythema and Eschar Formation:</u>	<u>Value</u>
No erythema.....	0
Very slight erythema (barely perceptible).....	1
Well-defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4

#### Edema Formation:

No edema.....	0
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (raised approximately 1 millimeter).....	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure).....	4

Fourteen days after treatment, the rabbits were killed with an air embolism and the organs of the thoracic and visceral cavities were examined for abnormalities.

### 4. RESULTS

Four rabbits died during the 14 days following administration of the test material. One, given 632 mg/kg was found dead on the morning of the third day, and three, given 2000 mg/kg, were found dead the morning after the application. There was no antemortem indication of systemic intoxication based on general appearance and behavior. The body weights of all survivors increased during the observation period.

The dermal LD50 calculated by the method of Litchfield and Wilcoxon is 1.1 g/kg with 95% confidence limits of 0.4 to 2.6 g/kg.

4. RESULTS (Continued)

There was no edema or eschar formation of the skin at any time. Three rabbits showed slight erythema for two to ten days. Hair growth appeared normal in the shaved area on the 14th day.

Necropsy findings were those commonly observed in untreated rabbits from this supplier as observed in our laboratory. No treatment-related abnormalities were noted.

5. CONCLUSIONS

Following the application of a single dose of DIMP to the abraded or intact skin of rabbits at doses of 0.2, 0.63, and 2.0 g/kg, only minimal indication of skin irritation was observed. Partial mortality (3/4) was seen at the highest dosage and one (of 4) died at the intermediate dosage.

PART I - SECTION I  
A TEST FOR LIVER ENZYME  
INDUCTION IN RATS

DIMP

LBI PROJECT NO. 2567

SUMMARY

The test material, DIMP, was administered orally to rats at 3000 ppm in the diet for 4 days. The duration of hexobarbital-induced sleeping time measured on the 5th day was larger in control than in DIMP-treated rats. Body weights and liver weights were not altered by treatment with DIMP. It was concluded that DIMP was a liver enzyme inducing agent.

1. OBJECTIVE

The purpose of this study was to test the potential of the test material to induce liver enzyme activity. The effect of pre-treatment of rats with the test material on hexobarbital induced sleep was used as a basis for this test.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Weanling Charles River COBS CD (SD) BR rats were received from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts. These test animals were housed individually in hanging wire cages and acclimated to laboratory conditions for 6 days. Water and diets were provided ad libitum.

The animals were assigned to treatment groups as indicated below:

<u>Group No.</u>	<u>Number of Rats</u>		<u>Treatment</u>
	<u>Male</u>	<u>Female</u>	
1	10	10	Control
2	10	10	3000 ppm DIMP

The test material was administered by incorporation into the basal diet (Purina Laboratory Chow Meal) at a level of 3000 ppm. The control rats received the basal ration.

3. EXPERIMENTAL DESIGN (continued)

All rats were observed frequently during the first 4 days of treatment for changes in general appearance and behavior. Body weights were obtained on Day 1 and 5 of the study.

On Day 5 of the study, 100 mg/kg of hexobarbital was administered by intraperitoneal injection to all rats and the duration of sleeping time was measured. The end point observed was based on the inability of the rat to right itself when placed on its side. After recovering from the effect of hexobarbital, all rats were killed with carbon dioxide, a gross necropsy performed, and the liver weighed.

4. RESULTS

There were no changes in general appearance of the rats during the first 4 days of treatment. Additional data (body weights, liver weights, and duration of sleeping time) have been tabulated in Table I-I-25. Analysis of these data suggested a difference between rats treated with DIMP and control rats. The sleep time of rats pretreated with DIMP was markedly reduced as compared to rats of the untreated group. This is the change expected following treatment with a liver enzyme inducing agent. However, the liver weight was not markedly increased as might have been expected with liver enzyme inducing agents.

Necropsy findings consisted of pale kidneys and mottled lungs. The frequency was similar in both treated and control rats.

5. CONCLUSIONS

DIMP was judged to be a liver enzyme inducing agent in rats.

TABLE I-I-25

## SUMMARY OF BODY WEIGHT, LIVER WEIGHT, AND SLEEPING TIME

ANIMAL NO. & SEX	BODY WEIGHT (g)		LIVER WEIGHT (g)	LIVER/BODY WEIGHT RATIO (%)	SLEEPING TIME (Minutes)
	Day 1	Day 5			
Group 1 - Control					
2042 M	79.1	90.4	6.928	7.66	23
2043 M	79.4	105.4	6.626	6.29	41
2044 M	81.0	106.2	6.044	5.69	38
2045 M	84.4	104.2	5.678	5.45	38
2046 M	82.6	111.3	5.936	5.33	23
2047 M	82.4	104.3	6.778	6.50	20
2048 M	71.6	98.1	5.102	5.20	33
2049 M	78.4	111.1	6.957	6.26	38
2050 M	87.2	114.1	7.753	6.79	44
2051 M	79.1	108.1	6.856	6.34	43
MEAN	80.52	105.32	6.466	6.15	32.30
S.E.	1.32	2.19	0.243	0.24	4.10
2052 F	71.1	92.1	5.026	5.46	50
2053 F	75.0	93.6	5.743	6.14	66
2054 F	75.6	99.4	7.225	7.27	54
2055 F	76.0	101.8	7.496	7.36	60
2056 F	72.7	94.8	4.998	5.27	48
2057 F	77.2	95.3	5.367	5.63	65
2058 F	78.1	100.6	6.879	6.75	59
2059 F	79.1	104.8	7.701	7.35	57
2060 F	73.1	88.5	5.147	5.82	51
2061 F	71.5	83.9	4.716	5.62	47
MEAN	74.94	95.48	6.030	6.27	56.20
S.E.	0.88	2.02	0.368	0.26	2.06

TABLE I-I-25 (Continued)  
SUMMARY OF BODY WEIGHT, LIVER WEIGHT, AND SLEEPING TIME

ANIMAL NO. & SEX	BODY WEIGHT (g)		LIVER WEIGHT (g)	LIVER/BODY WEIGHT RATIO (%)	SLEEPING TIME (Minutes)
	Day 1	Day 5			
Group 2 - DIMP					
2062 M	77.8	102.2	7.839	7.67	20
2063 M	81.3	110.7	7.100	6.41	12
2064 M	80.0	105.2	7.736	7.35	14
2065 M	82.8	112.1	7.317	6.53	9
2066 M	75.0	100.1	7.466	7.46	11
2067 M	79.1	103.2	5.585	5.41	20
2068 M	83.8	109.5	7.382	6.74	17
2069 M	80.3	108.2	5.959	5.51	22
2070 M	78.0	102.2	7.390	7.23	21
2071 M	84.4	110.6	6.754	6.11	12
MEAN	80.25	106.40	7.053	6.64	15.80
S.E.	0.93	1.37	0.235	0.25	1.50
2072 F	77.4	103.0	6.674	6.48	*
2073 F	74.4	97.7	6.548	6.70	13
2074 F	75.2	92.5	6.093	6.59	15
2075 F	73.6	91.4	5.785	6.33	8
2076 F	78.5	105.9	7.003	6.61	22
2077 F	75.1	97.8	6.649	6.80	*
2078 F	78.4	107.9	8.189	7.59	24
2079 F	70.3	96.9	6.938	7.16	18
2080 F	71.0	94.2	6.028	6.40	24
2081 F	73.9	97.5	5.782	5.93	23
MEAN	74.78	98.48	6.569	6.66	18.38
S.E.	0.89	1.74	0.229	0.14	2.10

\*Judged to have been incorrectly injected (did not sleep).

PART I - SECTION J  
GUINEA PIG SENSITIZATION

DIMP

LBI PROJECT NO. 2562

SUMMARY

DIMP should not be considered a strong sensitizer in guinea pigs.

1. OBJECTIVE

This study was designed to evaluate the sensitizing potential of the test material.

2. MATERIAL

Refer to Part I - Section A.

3. EXPERIMENTAL DESIGN

Twelve albino guinea pigs were obtained from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts, and randomly divided into two groups: four animals to receive a known sensitizing agent, 2,4-dinitro-1-chlorobenzene, and eight animals to receive the test material DIMP. The guinea pigs were housed individually with water and food available ad libitum.

Initially, and at intervals as needed thereafter, the hair was clipped from the trunk area. A 0.1% weight/volume solution of the known sensitizing material in physiological saline was injected intracutaneously on one side of the trunk area of each control animal. The control vehicle was injected into the other side of the trunk.

A 0.1% weight/volume solution of the test material in corn oil was injected intracutaneously into one side of the trunk of each test animal. The other side was injected with the vehicle only. The control and test materials were injected three times per week until a total of ten injections had been given.

Following the last sensitizing treatment, the animals were maintained for an additional two weeks, and then a challenge dose administered. The volume of injection was 0.05 ml for the first sensitizing injection, 0.1 ml for the balance of the sensitization exposure, and 0.05 ml for the challenge dose. The site of injection was examined for irritation 24 and 48 hours after each dose and was evaluated for erythema and edema according to the Draize scoring technique as follows:

### 3. EXPERIMENTAL DESIGN (Continued)

#### Draize Scoring Technique

##### Erythema

0 = none

1 = well defined

2 = moderate to severe

3 = severe to slight eschar formation

##### Edema

0 = none

1 = slight

2 = moderate (raised ca. 1.0 mm.)

3 = severe (raised 1.0 mm.)

The average diameter of the skin response was measured with calipers at 24 and 48 hours after administration of each dose. If the intensity of the local inflammatory response or the number of animals responding was substantially greater following the challenge injection than following the sensitizing injections, the material was considered to have produced sensitization.

### 4. RESULTS

Responses to initial injections of 2,4-dinitro-1-chlorobenzene ranged from zero to 5 x 5 mm in size and from no discoloration to a marked yellow-green color. Responses to the challenge injection, in all cases, were increased in area and degree of discoloration. The sizes were 2 to 15 (mathematically infinite) times the initial response in the same guinea pig. At the 48-hour observation, there was only slight reduction in response size.

Responses to initial injections of DIMP ranged from none (with no discoloration) to 4 x 4 mm with greenish color. With two exceptions the responses to challenge injections ranged from none (with no discoloration) to 7 x 8 mm with greenish discoloration (one with redness also). The other two showed were 10 x 12 mm and 8 x 10 mm, both greenish with red margins. In both of these, the size was substantially less at 48 hours.

### 5. CONCLUSIONS

DIMP should not be considered a strong sensitizer in guinea pigs.

PART I - SECTION K  
DEMYELINATION PARALYSIS IN CHICKENS

DIMP

LBI PROJECT NO. 2566

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NOT REPORTED AT THIS TIME--SEE FOREWORD

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PART I - SECTION L  
MICROBIAL MUTAGENESIS  
DIMP  
LBI PROJECT NO. 2568

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NOT REPORTED AT THIS TIME--SEE FOREWORD

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PART I - SECTION M  
PHARMACOKINETICS AND METABOLISM

DIMP

LBI PROJECT NO. 2569

SUMMARY

DIMP was absorbed following oral administration to mice, rats, and dogs. Peak plasma levels occurred in 15 minutes in mice and in two hours in rats and dogs. Storage of DIMP was found in the skin of mice and rats at 72 hours and in the gall bladder of dogs. Excretion appeared to be primarily via the urine in all three species, but there was some indication of biliary excretion in dogs. Eighty-five to 100% of the administered radioactivity appeared in urine and feces within 24 hours in all three species. Some 1 to 3% of the radioactivity in the urine was in the form of DIMP. The remainder appeared to be in the form of one major metabolite, in all three species. This metabolite was more polar than DIMP and was not conjugated.

1. OBJECTIVE

The purpose of this study was to determine the rate of absorption, tissue distribution, biotransformation, and time of excretion of Diisopropylmethyl [ $-^{14}\text{CH}_3$ ] phosphonate (DIMP- $^{14}\text{C}$ ) following a single oral dose given to mice, rats, and dogs.

2. MATERIAL

DIMP- $^{14}\text{C}$  (Lot No. 922-017), labeled in the methyl position with  $^{14}\text{C}$ , was synthesized by New England Nuclear Corporation, Boston, Massachusetts. The specific activity was 3.57  $\mu\text{Ci}/\text{mM}$  and the purity was greater than 99% as indicated by gas- and thin-layer chromatography. The total amount of 0.12 ml was diluted with 0.4 ml of nonradioactive DIMP, purchased from Richmond Organics, Richmond, Virginia. This stock of radiolabeled compound was analyzed for radiochemical purity by thin-layer chromatography using four different solvent systems. These results showed purity >97%. This stock of DIMP- $^{14}\text{C}$  was subsequently used for all pharmacokinetic and metabolism studies.

### 3. EXPERIMENTAL DESIGN

#### A. Animals and Administration of Radiolabeled DIMP-<sup>14</sup>C

##### 1. Mice

Thirty male, Swiss Webster mice, weighing 20 to 30 grams, were fasted for 18 hours and administered a single oral dose of DIMP-<sup>14</sup>C at 225 mg/kg of body weight. This solution contained 30 mg of DIMP-<sup>14</sup>C (specific activity 0.5  $\mu$ Ci/mg) per ml of polyethylene glycol (PEG 400). Three mice were housed in Roth [1] glass metabolic cages with free access to food and water. Animals received a normal diet of Purina Mouse Chow. The quantitative collection of urine, feces, and expired carbon dioxide was made at various time periods. The expired carbon dioxide was absorbed by a mixture containing ethanolamine:methylcellosolve:toluene (1:8:10 v/v).

##### 2. Rats

Fourteen male Sprague-Dawley rats, weighing 180 to 280 grams, were fasted for 18 hours and administered a single oral dose of DIMP-<sup>14</sup>C at 225 mg/kg of body weight. This solution contained 30 mg of DIMP-<sup>14</sup>C (specific activity 0.20  $\mu$ Ci/mg) per ml of PEG 400. Rats were housed individually in Roth metabolism cages with free access to food and water. Animals received a normal diet of Purina Rat Chow. The quantitative collection of urine, feces, and expired carbon dioxide was made at various time periods. The expired carbon dioxide was absorbed by a mixture containing ethanolamine:methylcellosolve:toluene (1:8:10 v/v).

##### 3. Dogs

Five male, young adult, purebred beagle dogs (Hazleton Laboratories, Cumberland, Virginia) weighing approximately 7.4 to 9.6 kilograms were used. The dogs were kept in individual stainless steel metabolism cages and received a normal diet of Purina Dog Chow throughout the entire study. The dogs were fasted for 18 hours and were given a single oral dose of DIMP-<sup>14</sup>C at 225 mg/kg body weight. This solution contained 45 mg of DIMP-<sup>14</sup>C (specific activity 0.01  $\mu$ Ci/mg) per ml of PEG 400.

### 3. EXPERIMENTAL DESIGN (Continued)

#### B. Sample Collection

##### 1. Blood

Three mice were killed by an intraperitoneal injection of sodium pentobarbital at 5, 15, and 30 minutes and at 1, 2, 4, 6, 24, 48, and 72 hours after administration of DIMP-<sup>14</sup>C. Two rats were similarly killed at 1, 2, 4, 6, 24, 48, and 72 hours. Blood was collected from the dorsal aorta in heparinized syringes. Blood from mice was pooled for each respective time. Blood was drawn from the femoral vein of dogs at 0.5, 1, 2, 4, 6, 10, and 24 hours after administration of DIMP-<sup>14</sup>C, and at each subsequent 24-hour interval until the dog was killed. Hematocrit values were determined for all samples and plasma was separated by centrifugation at 1500 to 2000 rpm for 15 minutes. Both blood and plasma were assayed for radioactivity.

##### 2. Urine, Feces, and Expired Carbon Dioxide

Urine, feces, and expired carbon dioxide were collected from mice and rats for 24 hours as indicated above and at 24-hour intervals thereafter until all animals were killed. Urine and feces were collected from individual dogs for each 24-hour interval until the dogs were killed by intravenous injection of Lidocaine at 4, 24, 48, and 72 hours and at 14 days after administration of DIMP-<sup>14</sup>C. Total volumes or weights were recorded and all samples were subjected to radioassay according to the procedure outlined in this report.

##### 3. Tissues and Organs

The following tissues and organs were excised from individual animals at each time stated above: spleen, lungs, heart, liver, kidneys, testes, brain, abdominal muscle, fat, urinary bladder, adrenals, eyes, femur, skin, gall bladder, small intestine, large intestine, cecum, and stomach. From dogs additional samples included: medulla, cerebrum, cerebellum, thyroid, lymph nodes, spinal cord, bone marrow, pancreas, pituitary, bile, lens, cornea, ocular fluid and ocular tissue. Tissues (100 to 200 mgs) were weighed directly into combustion cones or scintillation vials and processed for radioassay.

The contents of the stomach, small intestine, cecum, and large intestine were removed with normal saline and homogenized in a Virtis tissue homogenizer. Samples (100 to 200 mgs) were used for radioassay.

### 3. EXPERIMENTAL DESIGN (Continued)

#### B. Sample Collection

##### 3. Tissues and Organs

The stomach, small intestine, cecum, large intestine (without contents) and carcass of the animals were suspended in 30% NaOH for two to three days with constant stirring and then homogenized in a Virtis tissue homogenizer and Waring blender, respectively. Samples (100 to 200 mgs) were weighed directly into combustion cones or scintillation vials and processed for radioassay. All rat samples were processed individually while mice samples for each period were pooled, weighed, and treated as one sample.

#### C. Sample Preparation for Radioassay

Analysis of radioactive blood, plasma, urine, fecal homogenates, tissues, and tissue homogenates were performed by one of the following methods:

##### 1. Method I

This procedure is a modification of the method described by Mahin and Lofberg [2] in which xylene is substituted for toluene. Samples of blood, plasma, or urine (0.1 ml) and 100 to 200 mg of tissue, tissue homogenate, homogenate of gastrointestinal contents or fecal homogenate were placed directly into scintillation vials. All samples were run in triplicate. To the vials 0.2 ml 60% perchloric acid (analytical reagent) and 0.4 ml of 30% hydrogen peroxide were added. The samples were digested overnight in an oven at 65 to 70C. The vials were removed and allowed to cool to room temperature. The samples were mixed with 15 ml of scintillation solution. [This solution was made by dissolving 12.0 grams of 2,5-diphenyloxazole (PPO) (Packard Instrument Company) in 2 liters of xylene (Mallinkrodt).] Radioactive measurements were made after equilibration to 3C in a Tri-Carb liquid scintillation spectrometer, Model 3375, (Packard Instrument Company) or liquid scintillation spectrometer, LKB-8100. The  $^{14}\text{C}$  recovery was about 80% and  $^{14}\text{C}$  counting efficiency was in the range of 93 to 95%. All samples were counted with appropriate standards that were prepared by the same procedure. The counting time was selected to a statistical accuracy of  $1.0 \pm 2.5\%$ .

### 3. EXPERIMENTAL DESIGN (Continued)

#### C. Sample Preparation for Radioassay

##### 2. Method II

Some of the experimental samples were also processed using the Tri-Carb sample oxidizer Model 306, (Packard Instrument Company) [3]. Samples, as described under Method I, were placed directly into a combustion cone with an absorbing pad. A few drops of Combustaid (Packard Instrument Company) were added. The samples were combusted immediately at the appropriate settings for a 30-second combustion time. The resulting carbon dioxide was automatically trapped in sequence in 8 ml of carbosorb and 12 ml of permaflour V. The  $^{14}\text{C}$  recovery was in the range of  $98 \pm 1\%$  and  $^{14}\text{C}$  memory was less than 0.05%. The radioactive measurements were made after equilibration to 5C in a Tri-Carb liquid scintillation spectrometer, Model 3375 (Packard Instrument Company). The  $^{14}\text{C}$  counting efficiency was in the range of 93 to 95%. All samples were counted with appropriate standards that were prepared by the same procedure. The counting time was selected to yield a statistical accuracy of  $1.0 \pm 2.5\%$ .

##### 3. Preparation of Standards for Method I

Appropriate aliquots (0.1 or 0.2 ml) of DIMP- $^{14}\text{C}$  dosing solutions were placed into a 10 ml volumetric flask and diluted to 10 ml with methanol. Triplicate standards of 0.1 or 0.2 ml were then placed into scintillation vials. The standards were digested and counted as described in Method I along with the samples under investigation. Radioactivity present in the various test samples were quantitated in terms of  $\mu\text{g}$  of DIMP- $^{14}\text{C}$  per g or ml of wet tissue.

##### 4. Preparation of Standards for Method II

Appropriate aliquots (50  $\mu\text{l}$ ) of DIMP- $^{14}\text{C}$  dosing solutions were placed in triplicate into combustion cones. Standards were processed as described in Method II using the Tri-Carb sample oxidizer, Model 306 (Packard Instrument Company). Radioactivity measurements were made along with the test samples using a Tri-Carb liquid scintillation spectrometer, Model 3375 (Packard Instrument Company). Radioactivity present in the various test samples were quantitated in terms of  $\mu\text{g}$  of DIMP- $^{14}\text{C}$  per g or ml of wet tissue.

### 3. EXPERIMENTAL DESIGN (Continued)

#### D. Radioassay of Expired Carbon Dioxide

Expired carbon dioxide from mice and rats was absorbed by a mixture of ethanolamine:methylcellosolve:toluene (1:8:10 v/v). Five ml of this mixture were placed in triplicate into scintillation vials. Ten ml of scintillation solution was added. The blank sample consisted of 5 ml of ethanolamine-methylcellosolve-toluene and 10 ml of scintillation solution. The samples were measured for radioactivity with an appropriate standard taken in 5 ml of ethanolamine-methylcellosolve-toluene. The counting time was selected to yield a statistical accuracy of  $1.0 \pm 2.5\%$ .

#### E. Extraction of Radioactivity from Urine

Ten to 20 ml of 0- to 24-hour urine samples and control urine spiked with DIMP- $^{14}\text{C}$  (pH = 6-7) were extracted three times with equal volumes of chloroform. The chloroform layer was separated from extracted urine after centrifugation for 10 minutes at 1500 to 2000 rpm. The pooled volumes of chloroform and extracted urine were recorded. The original urine, the urine after extraction, and the chloroform extract were analyzed for radioactivity according to Method I. The resulting counts per minute were used to determine the percent radioactivity extracted by the solvent.

The chloroform extracts were evaporated to dryness using a Buchler flash rotary evaporator and then residues were taken up in small volumes of methanol. These samples were further analyzed by thin-layer chromatography to determine the nature of the radioactive components.

#### F. Enzymatic Hydrolysis of Urine

Glusulase (0.1 ml) was added to 10 ml of 0- to 24-hour urine sample and control urine spiked with DIMP- $^{14}\text{C}$ . [The activity of the glusulase was tested qualitatively using glucuronide phenolphthalein as a substrate. Glusulase (0.1 ml) contained 10,242 units of sulfatase and 19,717 units of  $\beta$ -glucuronidase (Lot No. HA043B, Endo Research Laboratories, Inc., Garden City, New York).] The urine samples were incubated in a constant temperature water bath at 37C for 24 hours. After incubation, the urine samples were extracted three times with equal volumes of chloroform. The original urine, extracted urine, and chloroform extracts were analyzed by liquid scintillation counting to determine the percent radioactivity in the various fractions. The chloroform extracts were then evaporated to

### 3. EXPERIMENTAL DESIGN (Continued)

#### F. Enzymatic Hydrolysis of Urine

dryness using a Buchler flash rotary evaporator and the residues were taken up in small volumes of methanol. The chloroform extracts were subjected to thin-layer chromatography to determine the nature of the radioactive components.

#### G. Thin-Layer Chromatography of Urine

All solvents used for thin-layer chromatography (TLC) studies were analytical grade reagents. TLC plates (5 x 20 and 20 x 20 cm) were precoated with silica gel G to a thickness of 0.25 mm and 0.20 mm, respectively. [Batch No. 3633643 and Batch No. 3028572, Merck and Company, Inc., Rahway, New Jersey] Total counts of 2000 to 5000 cpm in 10 to 20 ml samples were spotted. Several solvent systems were used for developing the TLC plates (see Results). The radioactive spots on the TLC plates (5 x 20 cm) were localized by scanning with a radiochromatogram scanner, Model 7201, (Packard Instrument Company) at appropriate settings for time constant (20 seconds), linear range (300 cpm), and chart speed (0.2 cm/min). Radioactivity present in each peak area was quantitated by means of a disc integrator. Radioactive spots on two dimensional TLC plates (20 x 20 cm) were localized by placing the plates on HQ-1000 X-ray film in a 8" x 10" cassette for 1 to 2 weeks. The films were developed and tracings were made of the radioactive spots that showed up on the film. In order to quantitate the radioactivity, the radioactive zones were scraped directly into scintillation vials. First the silica gel was suspended in 0.5 ml methanol and later 15 ml of scintillation fluid was added. The samples were counted and the radioactivity was calculated as percent in each zone.

### 4. RESULTS AND DISCUSSION

#### A. Blood and Plasma

The average blood and plasma levels for mice, rats, and dogs after administration of DIMP-<sup>14</sup>C are presented in Table I-M-26. The average plasma levels of DIMP-<sup>14</sup>C derived radioactivity were higher than blood levels at all times in all three species. The average peak plasma levels were 172.32 µg/ml at 15 minutes in mice, and 150.82 µg/ml, and 276.41 µg/ml at 2 hours in rats and dogs, respectively. These results indicate that DIMP-<sup>14</sup>C is absorbed more rapidly in mice than in rats or dogs. The average plasma values of DIMP-<sup>14</sup>C for all three species were plotted on semilogarithmic paper as µg/ml versus

#### 4. RESULTS AND DISCUSSION

##### A. Blood and Plasma (Continued)

time in hours. These results are presented in Figures I-M-1, I-M-2, and I-M-3. There appears to be two separate components with different half-lives and disappearance rates in all three species. The first set of components disappeared from plasma with  $T_1 1/2 = 30$  minutes in mice, 2.5 hours in rats and 1 hour in dogs with respective disappearance rate constants of  $K_1 = 1.39, 0.28, \text{ and } 0.69 \text{ hours}^{-1}$ . The second set of components had half-lives of  $T_2 1/2 = 32, 17.5 \text{ and } 21 \text{ hours}^{-1}$  with respective disappearance rate constants of  $K_2 = 0.02, 0.04 \text{ and } 0.03 \text{ hours}^{-1}$  for mice, rats and dogs, respectively. These results indicate that the parent DIMP- $^{14}\text{C}$  remains in the plasma for a relatively short time, but an unknown metabolite may be present for approximately 24 hours.

##### B. Tissue Distribution in Mice

The results of the distribution of radioactivity in tissues of mice at various times after oral administration of DIMP- $^{14}\text{C}$  are shown in Table I-M-27. The radioactivity was widely distributed with high levels observed in all tissues at 15 minutes after DIMP- $^{14}\text{C}$  administration. The highest levels were found in the urinary bladder, liver, lungs, and kidneys. After one hour DIMP- $^{14}\text{C}$  levels declined rapidly in all tissues except the urinary bladder and gall bladder. Still measurable amounts of radioactivity were detected in most of the tissues at 72 hours after administration of DIMP- $^{14}\text{C}$ . The highest levels found at 72 hours were in the skin. These results are in agreement with the absorption and half-life patterns shown in Figure I-M-1.

TABLE I-M-26

Average Plasma and Whole Blood Levels of  $^{14}\text{C}$  Radioactivity  
in Mice, Rats, and Dogs After a Single Oral Dose of  
225 mg/kg of DIMP- $^{14}\text{C}$

Hours After Treatment	$\mu\text{g/ml}$ of $^{14}\text{C}$ Radioactivity Calculated as DIMP- $^{14}\text{C}$					
	Mice		Rats		Dogs	
	Blood	Plasma	Blood	Plasma	Blood	Plasma
1/12	36.81	41.22	-	-	-	-
1/4	157.36	172.36	-	-	-	-
1/2	119.20	141.86	-	-	90.96	174.83
1	125.03	158.82	142.31	129.43	101.85	208.66
2	25.42	30.40	131.19	150.82	121.31	276.41
4	5.17	5.50	102.87	90.00	63.32	114.45
6	0.96	1.13	27.25	35.26	28.25	34.43
24	0.47	0.63	0.48	0.61	5.45	3.60
48	0.15	0.20	0.27	0.23	4.12	0.97
72	<0.01	0.05	0.37	0.11	2.12	0.45

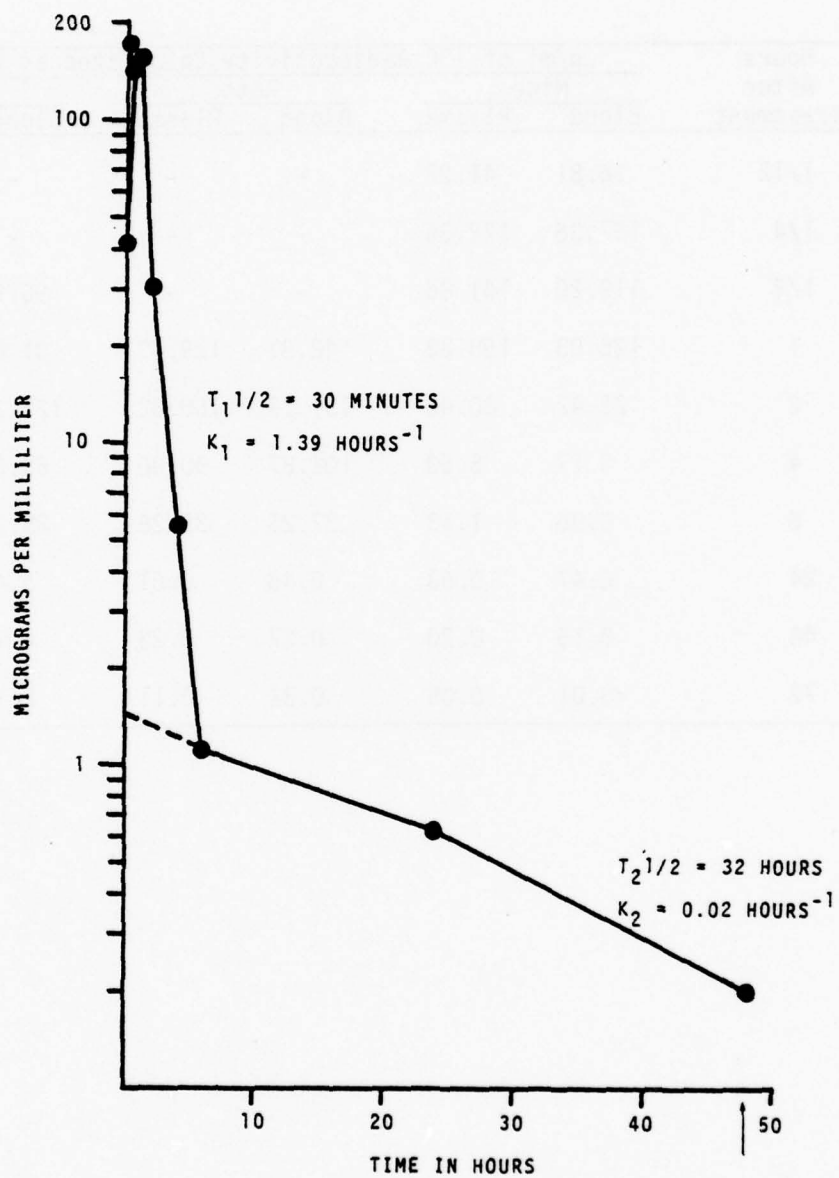


Figure I-M-1. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DIMP- $^{14}\text{C}$   $\mu\text{g/ml}$  in mice versus hours after administration of a single oral dose of 225 mg/kg of DIMP- $^{14}\text{C}$ .

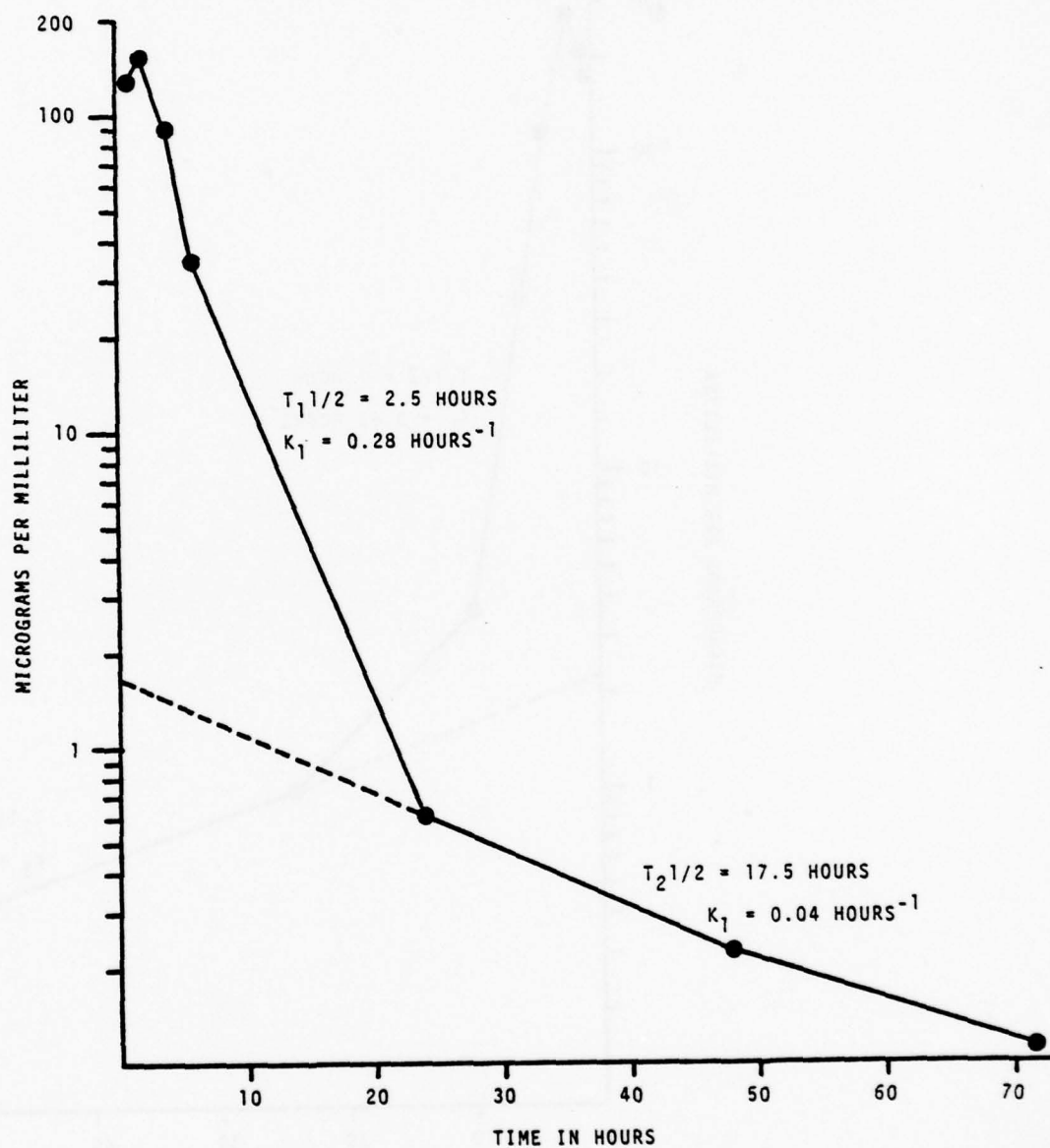


Figure I-II-2. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DIMP- $^{14}\text{C}$   $\mu\text{g/ml}$  in rats versus hours after administration of a single oral dose of 225 mg/kg of DIMP- $^{14}\text{C}$ .

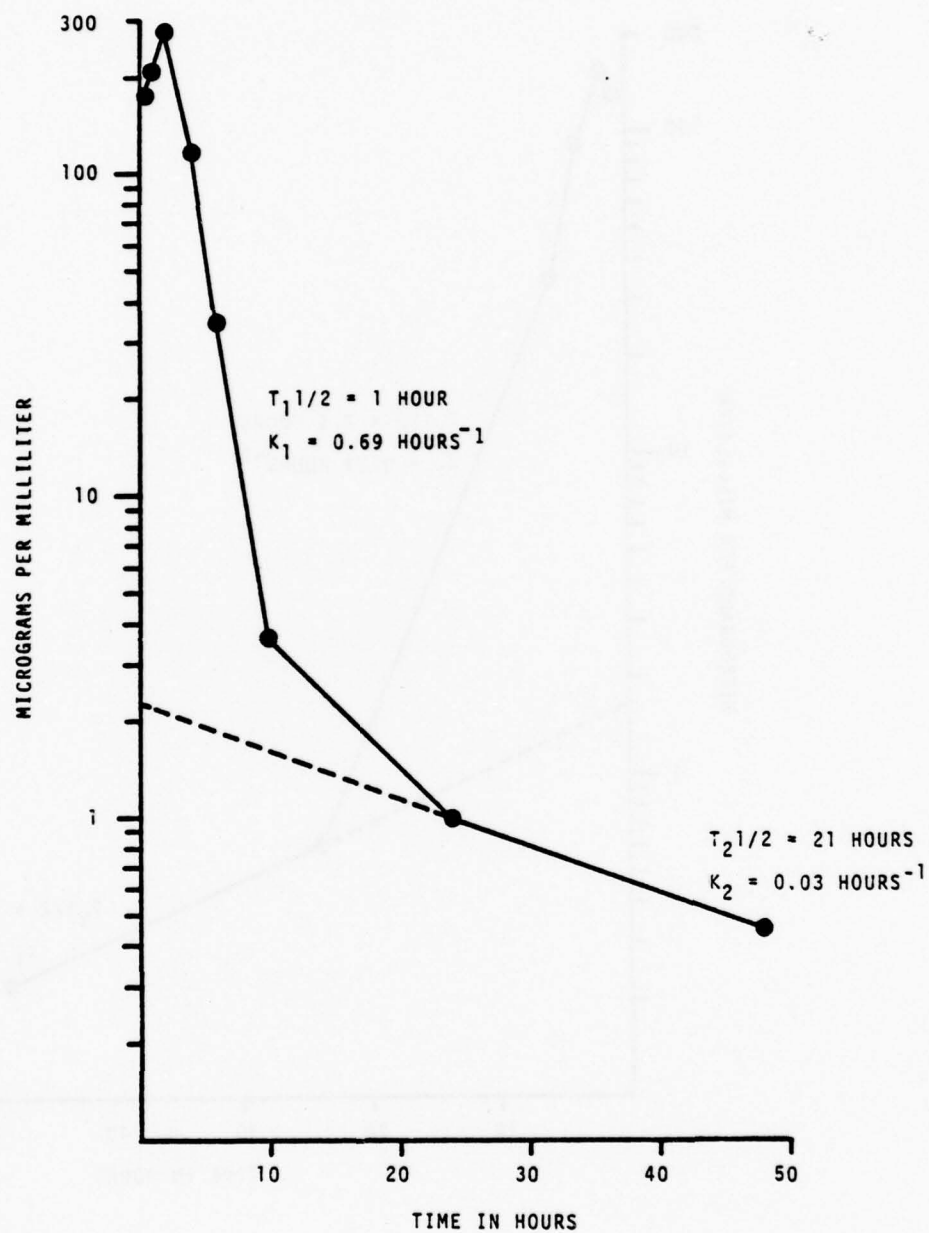


Figure I-M-3. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DIMP- $^{14}\text{C}$   $\mu\text{g/ml}$  in dogs versus hours after administration of a single oral dose of 225 mg/kg of DIMP- $^{14}\text{C}$ .

TABLE I-M-27

Tissue Distribution  $^{14}\text{C}$  Radioactivity ( $\mu\text{g/g}$  or  $\text{ml}$ ) in Mice at Various  
Time Periods After Administration of a Single Oral Dose of  
225  $\text{mg/kg}$  of DIMP- $^{14}\text{C}$

Tissue	Mg of $^{14}\text{C}$ Radioactivity Per Gram or ml Wet Tissue Calculated as DIMP- $^{14}\text{C}$ *									
	5 min	15 min	30 min	1 hr	2 hrs	4 hrs	6 hrs	24 hrs	48 hrs	72 hrs
Spleen	144.06	203.72	104.60	109.24	25.03	15.47	5.69	1.28	0.42	0.10
Lungs	104.06	321.87	318.02	351.29	100.51	30.91	15.77	2.13	0.67	0.29
Heart	60.73	185.19	114.01	104.72	26.93	13.45	7.78	2.44	0.66	0.46
Liver	272.64	568.87	393.62	343.44	88.31	11.73	2.08	0.64	0.41	0.29
Kidneys	85.09	313.59	302.84	319.91	109.26	33.61	7.13	1.62	0.55	0.14
Testes	18.26	135.07	87.80	77.77	18.73	11.07	2.59	1.26	0.33	0.15
Brain	45.89	167.97	80.37	59.99	9.28	1.66	1.14	0.47	0.12	0.12
Abdominal Muscle	55.47	170.97	99.85	114.86	19.46	14.80	2.98	1.11	4.36	0.30
Fat	99.10	132.92	73.02	103.90	20.51	13.93	3.65	1.69	0.99	<0.01
+Urinary Bladder	32.70	793.65	1145.47	1679.41	1083.00	1132.78	72.51	14.08	9.20	0.26
Adrenals	71.70	212.89	122.18	156.26	35.34	11.67	16.00	2.25	0.57	<0.01
Eyes	25.34	136.03	92.97	89.87	24.39	8.87	4.20	0.81	0.27	0.26
Femur	20.43	97.39	62.06	91.84	13.39	8.29	5.61	0.93	0.29	0.24
Skin	25.25	150.20	115.09	145.66	35.67	19.73	5.15	6.86	4.65	7.16
Gall Bladder	83.78	260.91	275.35	322.52	131.58	291.23	8.60	1.17	1.78	0.18

\*The values shown represent the average of the organs of three mice at each time period.

+Without content.

#### 4. RESULTS AND DISCUSSION (Continued)

##### C. Tissue Distribution in Rats

The results of the distribution of radioactivity in tissues of rats at various times after administration of DIMP- $^{14}\text{C}$  are shown in Table I-M-28. The radioactivity was widely distributed with high levels found in all tissues at 1 and 2 hours. The highest levels were again found in the urinary bladder, lungs, liver, and kidneys. Radioactivity declined in all tissues except the urinary bladder after 2 hours, but the rate was slower in rat tissue than in mouse tissue. Radioactivity was detected in all tissues at 72 hours, and the highest level present at this time was in skin. These results are consistent with the absorption and half-life patterns shown in Figure I-M-2.

##### D. Tissue Distribution in Dogs

The distribution of radioactivity in tissues of dogs at various times after administration of a single oral dose of DIMP- $^{14}\text{C}$  are presented in Table I-M-29. The radioactivity was widely distributed in all tissues, but the highest levels were found in bile, liver, gall and urinary bladders at 4 hours after administration of DIMP- $^{14}\text{C}$ . At 24 hours, DIMP- $^{14}\text{C}$  levels were found in the lungs, bone marrow, cecum, and urinary bladder. These results suggest the possibility of limited biliary excretion in dogs although the primary route of excretion of DIMP- $^{14}\text{C}$ -derived compounds in mice and rats is via the urine.

The distribution of radioactivity in various sections of the individual eyes of dogs is summarized in Table I-M-30. These results show that the highest concentration of radioactivity was located in the whole eye (all parts) at 4 hours after administration of DIMP- $^{14}\text{C}$ . After that time radioactivity was greatly reduced. At 72 hours radioactivity was detected in the right lens but this finding is probably an artifact.

##### E. Percentage of Excretion

The percentage of radioactivity recovered in urine, feces, the gastrointestinal tract, expired air, and the carcass of mice and rats is presented in Tables I-M-31 and I-M-32, respectively. Similar data from dogs also including the percentage of radioactivity recovered in excised organs, bile, blood, and muscle are given in Table I-M-33. The primary route of excretion of DIMP- $^{14}\text{C}$  (or metabolites) appears to be through the urine in all three species.

TABLE I-M-28

Tissue Distribution of  $^{14}\text{C}$  Radioactivity ( $\mu\text{g/g}$  or  $\text{ml}$ ) in Rats at Various Time Periods After Administration of a Single Oral Dose of 225  $\text{mg/kg}$  of DIMP- $^{14}\text{C}$

Tissue	$\mu\text{g}$ of $^{14}\text{C}$ Radioactivity Per Gram or $\text{ml}$ Wet Tissue Calculated as DIMP- $^{14}\text{C}$						
	1 hr	2 hrs	4 hrs	6 hrs	24 hrs	48 hrs	72 hrs
Spleen	119.29	107.05	70.87	22.48	1.00	0.12	0.70
Lungs	471.82	658.76	625.92	287.80	1.75	0.26	0.26
Heart	128.07	101.59	71.10	22.87	2.12	0.45	0.15
Liver	476.06	577.68	538.11	186.58	2.10	0.58	0.63
Kidneys	312.34	317.27	300.86	172.82	3.37	1.15	0.79
Testes	119.21	99.70	56.95	19.25	1.12	0.33	0.28
Brain	117.94	101.10	52.85	5.73	0.44	0.20	0.15
Abdominal Muscle	116.87	102.27	64.13	14.68	1.06	0.32	0.18
Fat	100.82	80.38	48.94	10.96	1.27	0.56	0.63
†Urinary Bladder	253.97	927.73	2028.22	1226.03	23.62	1.08	0.74
Adrenals	154.24	174.08	103.74	19.42	1.21	0.39	0.27
Eyes	101.14	97.55	84.17	17.89	0.70	0.18	0.27
Femur	65.21	69.18	47.90	11.09	0.64	0.11	0.19
Skin	117.83	97.00	73.61	24.06	1.60	3.86	6.31

\*The values shown represent average of two rats at each time period.

†Without content.

TABLE I-M-29

Tissue Distribution of  $^{14}\text{C}$  Radioactivity ( $\mu\text{g}$  per gram or per ml) in Male  
Dogs at Various Time Periods After Administration of a  
Single Oral Dose of 225 mg/kg of DIMP- $^{14}\text{C}$

Tissue	$\mu\text{g}$ of $^{14}\text{C}$ Radioactivity Per Gram or ml Wet Tissue Calculated as DIMP- $^{14}\text{C}$				
	4 hrs	24 hrs	48 hrs	72 hrs	2 weeks
Spleen	33.24	5.39	<0.01	<0.01	<0.1
Lungs	86.02	10.89	0.02	<0.01	<0.1
Heart	23.83	4.55	<0.01	<0.01	<0.1
Liver	335.49	7.67	0.34	0.46	<0.1
Kidneys*	83.84	7.67	0.13	<0.01	<0.1
Testes*	12.31	6.18	0.97	0.19	<0.1
Medulla	1.52	0.30	0.04	<0.01	<0.1
Cerebrum	2.36	3.71	<0.01	<0.01	<0.1
Cerebellum	2.11	4.33	<0.01	<0.01	<0.1
Urinary Bladder*	211.98	8.88	0.85	<0.01	<0.1
Adrenals*	24.48	0.45	<0.01	<0.01	<0.1
Eyes*	11.97	5.17	<0.01	<0.01	<0.1
Femur	0.01	7.18	<0.01	<0.01	<0.1
Skin	17.97	4.10	<0.01	-	<0.1
(Sk+Ab) Muscle†	11.14+42.28	4.91	<0.01	-	<0.1
Bile	529.01	2.29	1.48	0.18	<0.1
Fat	11.81	6.93	<0.01	-	<0.1
Thyroid	17.68	0.80	<0.01	-	<0.1
Lymph Nodes	22.23	2.45	<0.01	<0.01	<0.1
Stomach**	19.05	0.70	<0.01	<0.01	<0.1
Small Intestine**	21.47	2.01	<0.01	2.08	<0.1
Cecum**	4.50	10.12	6.41	<0.01	<0.1
Large Intestine**	20.06	7.09	1.32	<0.01	<0.1
Spinal Cord	3.28	4.52	<0.01	<0.01	<0.1
Bone Marrow	12.57	10.13	<0.01	-	<0.1
Pancreas	20.61	0.37	<0.01	-	<0.1
Pituitary	23.83	<0.01	<0.01	<0.01	<0.1
Gall Bladder	219.98	4.63	-	1.14	<0.1

Detection limit  $\pm 0.1 \mu\text{g}/100\text{-}200 \mu\text{mg}$  tissue.

\*Value is average of two organs.

\*\*Tissue without content.

†Average of smooth and abdominal muscle values.

TABLE 1-11-30  
Distribution of  $^{14}\text{C}$  Radioactivity in Various Sections of Individual Eyes of Male  
Dogs After Administration of a Single Oral Dose of 225 mg/kg of DIMP- $^{14}\text{C}$

Kill Time	Tissue Section	$\mu\text{g/g}$	Section Weight g	$\mu\text{g/Section}$	$\mu\text{g/g for Whole Eye}$	Total $\mu\text{g/Eye}$	% Dose/Organ
4 hrs	Right: Cornea	15.10	<0.1	0.45			
	Lens	13.33	0.32	4.27			
	Fluid	11.84	3.21	37.99			
	Ocular Tissue	17.49	1.22	21.33	11.97	64.04	<0.01
	Left: Cornea	14.49	<0.1	0.29			
	Lens	5.09	0.22	1.12			
24 hrs	Ocular Fluid	10.07	3.20	32.22			
	Right: Tissue	14.96	1.34	20.05	10.09	53.68	<0.01
	Cornea	0.39	0.14	<0.1			
	Lens	0.60	0.46	0.27			
	Fluid	1.73	2.50	4.33	1.36	6.59	<0.01
	Ocular Tissue	1.63	1.19	1.94			
48 hrs	Left: Cornea	1.32	0.15	0.20			
	Lens	0.63	0.43	0.27			
	Fluid	1.16	2.92	3.39	1.47	7.05	<0.01
	Ocular Tissue	2.87	1.11	3.19			
	Right: Cornea	<0.1	0.17	<0.1			
	Lens	<0.1	0.35	<0.1	<0.01	<0.01	<0.01
72 hrs	Fluid	<0.1	2.38	<0.1			
	Ocular Tissue	<0.1	1.09	<0.1			
	Left: Cornea	<0.1	<0.1	<0.1	<0.1	<0.1	<0.01
	Lens	<0.1	0.31	<0.1			
	Fluid	<0.1	2.36	<0.1			
	Ocular Tissue	<0.1	1.17	<0.1			
2 weeks	Right: Cornea	<0.01	0.13	<0.1			
	Lens	114.35	0.42	48.03	10.33	50.41	<0.01
	Fluid	1.05	2.01	2.11			
	Ocular Tissue	0.18	1.50	0.27			
	Left: Cornea	0.23	0.20	0.05			
	Lens	<0.1	0.46	<0.1	0.45	2.34	<0.01
	Fluid	0.60	2.23	1.34			
	Ocular Tissue	0.62	1.55	0.95			
	Right: Cornea	0.72	0.16	0.12			
	Lens	0.23	0.35	<0.10			
	Fluid	0.23	3.04	0.69	0.25	1.34	<0.01
	Ocular Tissue	0.36	1.25	0.45			
	Left: Cornea	<0.1	0.30	<0.1			
	Lens	0.37	0.29	0.11	0.27	1.43	<0.01
	Fluid	0.32	2.90	0.93			
	Ocular Tissue	0.34	1.15	0.39			

TABLE I-M-31

Percent of  $^{14}\text{C}$  Radioactivity Recovered in Urine, Feces, Carcass,  
Gastrointestinal Tract and Expired Air by Mice at Various Time  
Periods After Administration of a Single Oral Dose of  
225 mg/kg of DIMP- $^{14}\text{C}$

Time in Hours	% $^{14}\text{C}$ Radioactivity Recovered Calculated as DIMP- $^{14}\text{C}$					
	Urine	Feces	Carcass	GI Tract Tissue & Contents	Expired Air	Total
1/12	<0.01	<0.01	19.79	53.35	None	73.16
1/4	0.31	None	38.24	57.45	0.29	96.29
1/2	17.16	<0.01	28.40	41.22	0.05	86.83
1	47.70	None	30.08	13.27	0.10	91.15
2	49.54	4.22	8.91	14.12	0.23	77.02
4	97.82	2.91	3.57	2.07	<0.01	106.37
6	101.11	3.93	1.75	1.49	0.43	108.71
24	78.23	7.76	2.09	2.88	0.20	91.16
48	72.69	7.90	1.02	1.61	0.37	83.59
72	95.32	29.25	0.60	1.00	-	126.17

- The value for expired air was not determined.

TABLE I-M-32

Percent of  $^{14}\text{C}$  Radioactivity Recovered in Urine, Feces, Carcass,  
Gastrointestinal Tract and Expired Air by Rats at Various Time  
Periods After Administration of a Single Oral Dose of  
225 mg/kg of DIMP- $^{14}\text{C}$

Time in Hours	% $^{14}\text{C}$ Radioactivity Recovered*					Total
	Urine	Feces	Carcass	GI Tract Tissue & Contents	Expired Air	
1	4.36	None	23.87	50.46	0.05	78.74
2	17.07	3.09	26.92	39.16	0.14	86.38
4	45.25	2.75	17.67	29.47	0.53	95.67
6	34.65	2.63	9.49	14.08	0.08	60.93 <sup>†</sup>
24	91.72	10.14	1.40	2.65	0.12	106.03
48	88.83	15.75	1.12	0.72	0.41	106.83
72	85.90	20.84	0.47	0.23	0.34	107.78

\*The values shown represent average of two rats at each time period.

<sup>†</sup>The low is appeared to be due to the loss of urine.

TABLE I-M-33

Percent  $^{14}\text{C}$  Radioactivity Recovered From Male Dogs at Various Time Periods  
After Administration of a Single Oral Dose of 225 mg/kg of DIMP- $^{14}\text{C}$

Time In Hours	Percent $^{14}\text{C}$ Radioactivity Recovered Calculated as DIMP- $^{14}\text{C}$					
	Urine	Feces	GI Tract Contents	Excised Organs	Bile	* Blood    ** Muscle    Total
4 hrs	13.48	None	1.40	6.74	0.06 (2.55)	1.47    1.49    23.89
24 hrs	86.25	1.99	0.21	0.29	<0.01 (7.05)	0.01    0.65    89.40
48 hrs	93.00	0.56	<0.01	<0.01	<0.01 (6.66)	<0.01    <0.01    93.56
72 hrs	97.13	0.64	<0.01	0.04	<0.01 (6.10)	0.10    0.05    97.96
2 weeks	85.46	3.24	<0.01	0.07	<0.01 (5.68)	<0.01    0.06    90.30

Body Weights and Administered Dose - 4 9.6 kg 2160 mgs  
5 7.4 kg 1665 mgs  
6 7.6 kg 1710 mgs  
1 7.4 kg 1665 mgs  
2 7.2 kg 1620 mgs

\*Blood values are calculated as 9% of the body weight.

\*\*Muscle values are calculated as 30% of the body weight.

( ) Values in parentheses indicate weights of bile in grams.

#### 4. RESULTS AND DISCUSSION (Continued)

##### E. Percentage of Excretion

Marked differences did occur in the rate of excretion of  $^{14}\text{C}$  in urine with mice, reaching maximum excretion at 6 hours, rats at 24 hours, and dogs at 72 hours. Approximately 85 to 100% of all radioactivity was recovered in all three species in the urine and feces within 24 hours after a single oral dose of DIMP- $^{14}\text{C}$ . Small amounts of  $^{14}\text{C}$  were also detected in the expired air from mice and rats. The exact nature of this component was not determined, but it may be a product of the demethylation of DIMP- $^{14}\text{C}$  leading to radioactive carbon dioxide. Regardless, this route of excretion cannot be considered as the major metabolic pathway.

##### F. Metabolic Fate of DIMP- $^{14}\text{C}$ in Mice, Rats, and Dogs

The 0- to 24-hour urines from mice, rats, and dogs were analyzed by thin-layer chromatography (TLC). The results of the initial TLC analyses are shown in Table I-M-34. Urine from mice and rats showed three radioactive components while the dog urine showed only one component. The major component present in all three species, designated as I, contained 96 to 100% of the radioactivity and did not move from the origin. The other two components with varying polarity had  $R_f$  values of: Mouse II,  $R_f = 0.07$  (1.4%) and III  $R_f = 0.21$  (1.4%); Rat II,  $R_f = 0.13$  (2.5%) and III  $R_f = 0.27$  (1.10%). The  $R_f$  value of DIMP- $^{14}\text{C}$  under identical conditions was found to be 0.23. In order to achieve complete resolution of the radioactive components, the same urine samples were subjected to two dimensional TLC with two diverse solvent systems. These results are shown in Table I-M-35. The urine from mice and rats showed three components which confirms the earlier results; however, an additional component was detected for dog urine. The experiments were performed similarly for 0- to 24-hour urines spiked with DIMP- $^{14}\text{C}$ . The results of these analyses showed that none of three components corresponded to urines spiked with DIMP- $^{14}\text{C}$ . The 0- to 24-hour urines from mice, rats, dogs, and control urine spiked with DIMP- $^{14}\text{C}$  were extracted with chloroform at pH = 6-7, and these data are shown in Table I-M-36. Approximately 1 to 3% of the total radioactivity was extracted into chloroform from urine of all three species, whereas DIMP- $^{14}\text{C}$  was 98% extractable into chloroform from control urine spiked with DIMP- $^{14}\text{C}$ . These results indicate the presence of 1 to 3% nonmetabolized DIMP- $^{14}\text{C}$  in the urine of all three species with a high percentage of other metabolites.

TABLE I-II-34

Percent  $^{14}\text{C}$  Radioactivity Associated With Different Components Resolved  
by One Dimensional Thin-layer Chromatography of 0-24 Hour Mouse, Rat,  
and Dog Urine After Administration of a Single Oral Dose of  
225 mg/kg of DIMP- $^{14}\text{C}$

Sample	Component	Rf	% Radioactivity In Each Component
DIMP- $^{14}\text{C}$	DIMP- $^{14}\text{C}$	0.23	100.00
0-24 Hour Mouse Urine	I	0.00	97.20
	II	0.07	1.40
	III	0.21	1.40
0-24 Hour Rat Urine	I	0.00	96.40
	II	0.13	2.50
	III	0.27	1.10
0-24 Hour Dog Urine	I	0.00	100.00

Developing solvent system: Chloroform:Acetone (17:3 v/v)

TABLE I-M-35

Percent  $^{14}\text{C}$  Radioactivity Associated With Different Components Resolved  
by Two Dimensional Thin-layer Chromatography of 0-24 Hour Mouse, Rat,  
and Dog Urine After Administration of a Single Oral Dose of  
225 mg/kg of DIMP- $^{14}\text{C}$

Sample	Component	Rf*	% Radioactivity In Each Component
DIMP- $^{14}\text{C}$	DIMP- $^{14}\text{C}$	0.94	100.0
0-24 Hour Mouse Urine	I	0.58	96.0
	II	0.74	2.5
	III	0.82	1.5
0-24 Hour Rat Urine	I	0.86	93.2
	II	0.87	4.3
	III	0.91	2.5
0-24 Hour Dog Urine	I	0.65	94.0
	II	0.75	6.0

\*From Solvent 2.

Solvent 1: Chloroform:Acetone (17:3 v/v)

Solvent 2: Methanol: $\text{NH}_4\text{OH}$ :Trichloroacetic acid:Water (10:3:1:6 v/v)

TABLE I-M-36

Percent  $^{14}\text{C}$  Radioactivity Extracted Into Chloroform From 0-24 Hour Mouse, Rat, and Dog Urine After Administration of a Single Oral Dose of 225 mg/kg of DIMP- $^{14}\text{C}$

Sample	% $^{14}\text{C}$ Extracted In Chloroform	% $^{14}\text{C}$ Remaining In Urine	Total % $^{14}\text{C}$ Recovered
Chloroform Extract Control Urine Spiked With DIMP- $^{14}\text{C}$	98.37	1.63	100.00
Chloroform Extract 0-24 Hour Mouse Urine	3.23	95.97	99.20
Chloroform Extract 0-24 Hour Rat Urine	2.80	96.30	99.10
Chloroform Extract 0-24 Hour Dog Urine	1.10	99.00	101.10

#### 4. RESULTS AND DISCUSSION (Continued)

##### F. Metabolic Fate of DIMP-<sup>14</sup>C in Mice, Rats, and Dogs

The 0- to 24-hour urines from mice, rats, dogs, and a control urine spiked with DIMP-<sup>14</sup>C were subjected to enzymatic hydrolysis with glucuronidase and then extracted with chloroform. The data relating to the percent of radioactivity extractable into chloroform are summarized in Table I-M-37. The results show that the radioactivity extracted into chloroform did not increase following enzyme treatment. Therefore, enzymatic hydrolysis of the urine samples with  $\beta$ -glucuronidase or sulfatase did not occur indicating the absence of urine conjugates.

#### 5. LITERATURE CITED

- [1] Roth, L., Leifer, E., Hogness, T.B. and Langham, W.M.: Studies on the metabolism of radioactivity of nicotinic acid and nicotinamide in mice. *J. Biol. Chem.*, 176:249, 1948.
- [2] Mahin, D.T. and Lefberg, R.J.: *Anal. Biochem.*, 16:600, 1966.
- [3] Tri-Carb Sample Oxidizer 306 Manual 1 1975, Packard Instrument Company.

TABLE I-1-37

Percent  $^{14}\text{C}$  Radioactivity Extracted Into Chloroform From 0-24 Hour  
Mouse, Rat, and Dog Urine After Enzymatic Hydrolysis With Glusulase

Sample	% $^{14}\text{C}$ Extracted In Chloroform	% $^{14}\text{C}$ Remaining In Urine	Total % $^{14}\text{C}$ Recovered
Control Urine Spiked With DIMP- $^{14}\text{C}$ + $\text{G}_1$	106.00	0.00	106.00
0-24 Hour Mouse Urine + $\text{G}_1$	4.59	92.50	99.80
0-24 Hour Rat Urine + $\text{G}_1$	2.48	97.35	99.80
0-24 Hour Dog Urine + $\text{G}_1$	0.80	101.00	101.80

$\text{G}_1$  = Glusulase  $\beta$ -glucuronidase + sulfatase

PART II - SECTION A  
INTRODUCTION AND MATERIAL

DCPD

1. INTRODUCTION

The toxicity of DCPD has been studied acutely by the oral, dermal, and eye exposure routes in laboratory animals as well as in repeated subchronic exposure in rats, mice, and dogs. Special studies on liver enzyme induction activity and mutagenesis have also been conducted. From the information gathered, dosages can be set for evaluation of DCPD in chronic studies.

Preliminary information on the rate of absorption, distribution, and excretion has been gained from pharmacokinetic studies. This can be used as background for the further evaluation of metabolic fate. The pharmacokinetic studies together with the toxicity work can form an understanding of the safe use and risk of DCPD with respect to human exposure.

2. MATERIAL

DCPD (Dicyclopentadiene) also known as 3a,4,7,7a-Tetrahydro-4,7-methanoindene, was purchased from MC/B, 2909 Highland Avenue, Norwood, Ohio 45212, under catalog number TX 310. A single batch of 650 g was received on August 18, 1976, and assigned LBI No. 763A.

Analysis of DCPD was performed with a UC-W98 column. The retention time of the compound was 1.9 minutes. Trace impurities were noted at approximately 1.5 minutes and 2.1 minutes. The purity of DCPD appeared to be 98 to 99%, which is consistent with the MC/B assay of 99.79%. It cannot now be determined if one of these impurities may be the cis form.

Because of poor water solubility, DCPD was prepared for administration to animals by dissolving it in corn oil (Mazola) at concentrations appropriate to the various studies. The handling of DCPD itself was facilitated by slight warming, which converted the waxy solid to an easily measured liquid.

PART II - SECTION B  
ACUTE ORAL TOXICITY STUDY IN RATS

DCPD

LBI PROJECT NO. 2558

SUMMARY

The oral LD50 values of DCPD were calculated to be 520 (420-645) and 378 (303-473) mg/kg in male and female rats, respectively.

1. OBJECTIVE

The objective of this study was to evaluate the acute toxicity of DCPD when administered orally to rats.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Sprague-Dawley rats were received from ARS/Sprague-Dawley, Madison, Wisconsin. These test animals were housed individually in hanging wire cages and acclimated to laboratory conditions. Water and Purina Laboratory Chow (ground) were provided ad libitum with the exception of the night before treatment when the food was removed from the cages.

Single graded doses of the test material, DCPD, dissolved in corn oil (Mazola) at a concentration of 196 mg/ml, were administered by gastric intubation to the test animals. Following treatment, the animals were observed frequently on the day of treatment and daily thereafter.

The animals were weighed on the day of treatment, and on Days 7 and 14 following treatment. Gross necropsies were performed on all animals that died during the study and on the surviving animals that were killed 14 days after treatment.

#### 4. RESULTS

The data have been summarized as follows:

Dose (mg/kg)	Deaths					Total
	Day					Mortality
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5-14</u>	<u>Deaths/Treated</u>
<u>MALES</u>						
278	0	1	0	0	0	1/10
360	0	2	0	0	0	2/10
464	0	3	0	0	0	3/10
600	0	7	1	0	0	8/10
793	0	7	1	0	0	8/10
<u>FEMALES</u>						
278	0	0	0	0	0	0/10
360	0	5	0	0	0	5/10
464	0	7	0	0	0	7/10
600	0	9	0	0	0	9/10
793	0	10	0	0	0	10/10

The LD50 values (and 95% confidence limits) calculated by the method of Horn (Biometrics, 12:311, 1956) were 520 (420-645) mg/kg for male and 378 (303-473) mg/kg for female rats, respectively.

Signs of intoxication in both males and females included red stains around nose and mouth, decreased activity, occasional ataxia and prostration within one to four hours after dosing. Some instances of tremors and convulsions were reported and not all of these rats later died.

At necropsy of the survivors, all tissues appeared normal. Necropsy findings in animals of all levels dying during the study included hyperemia of the lungs, but most showed no abnormalities. The odor of DCPD was uniformly present.

#### 5. CONCLUSIONS

Following the oral administration of graded doses of DCPD to fasted male and female rats, the LD50 values were 520 (420-645) and 378 (303-473) mg/kg for males and females, respectively.

PART II - SECTION C  
ACUTE ORAL TOXICITY STUDY IN MICE

DCPD

LBI PROJECT NO. 2559

SUMMARY

The oral LD50 values of DCPD were calculated to be 190 (125-289) and 250 (170-368) mg/kg in male and female mice, respectively.

1. OBJECTIVE

The objective of this study was to evaluate the acute toxicity of DCPD when administered orally to mice.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Swiss Webster mice were received from Camm Research, Wayne, New Jersey. These test animals were housed in groups of five by sex in solid bottom plastic cages and acclimated to laboratory conditions. Water and Purina Laboratory Chow (ground) were provided ad libitum with the exception of the night before treatment when the food was removed from the cages.

Single graded doses of the test material, DCPD, dissolved in corn oil at a concentration of 10% v/v, were administered by gastric intubation to the test animals. Following treatment, the animals were observed frequently on the day of treatment and daily thereafter.

The animals were weighed on the day of treatment, and on Days 7 and 14 following treatment. Gross necropsies were performed on all animals that died during the study and on the surviving animals that were killed 14 days after treatment.

#### 4. RESULTS

The data have been summarized as follows:

<u>Dose</u> (mg/kg)	<u>Deaths</u> <u>Day</u>					<u>Total</u> <u>Mortality</u>
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5-14</u>	<u>Deaths/Treated</u>
<u>MALES</u>						
167	3	2	0	0	0	5/10
215	4	1	0	0	0	5/10
278	3	2	0	0	1	6/10
360	5	2	0	0	0	7/10
464	2	6	0	0	0	8/10
600	6	3	0	0	1	10/10
<u>FEMALES</u>						
167	0	0	0	0	0	0/10
215	3	3	0	0	0	6/10
278	2	1	0	0	0	3/10
360	2	7	0	0	0	9/10
464	3	2	0	0	0	5/10
600	4	5	0	0	0	9/10

The LD50 values (and 95% confidence limits) calculated by the method of Horn (Biometrics, 12:311, 1956) were 190 (125-289) and 250 (170-368) mg/kg for male and female mice, respectively.

Signs of intoxication in both males and females included decreased activity and prostration within one to four hours after dosing.

At necropsy of the survivors, all tissues appeared normal. Necropsy findings in animals of all levels dying during the study consisted of yellow fluid in the stomach and small intestines, distension of the bladder with pinkish-orange fluid, hyperemia of the lungs, and black discoloration of portions of the liver and spleen. Some of these changes may represent postmortem degeneration.

#### 5. CONCLUSIONS

Following the oral administration of graded doses of DCPD to fasted male and female mice, the LD50 values were 190 (125-289) and 250 (170-368) mg/kg for males and females, respectively.

PART II - SECTION D  
90-DAY TOXICITY STUDY IN RATS

DCPD

LBI PROJECT NO. 2563

SUMMARY

No evidence of toxicity resulted from dietary administration of DCPD to rats at levels of 80, 250, and 750 ppm for 90 days.

1. OBJECTIVE

The purpose of this study was to characterize the subchronic toxicity of DCPD by administration in the diet of rats over a 90-day period.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in rats obtained from ARS/Sprague-Dawley, Madison, Wisconsin, with body weights averaging 86.5 grams for males and 74.9 grams for females at initiation.

B. Animal Groups

The rats were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	30	30	Zero - Control
2	30	30	Low - 80 ppm
3	30	30	Medium - 250 ppm
4	30	30	High - 750 ppm

C. Diet Preparation

The rats were fed Purina Rat Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

### 3. EXPERIMENTAL DESIGN (Continued)

#### D. Observations

Body weights and food consumption were recorded weekly. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects. Entries were made in records only when abnormalities were noted.

#### E. Special Examinations

Ophthalmoscopic examination of each animal was performed by an experienced veterinarian before compound administration was begun and again during the final week of the study.

#### F. Clinical Laboratory Measurements

The following determinations were made on five rats of each sex from the control and each test level:

	<u>4 Wks</u>	<u>13 Wks</u>
<u>Hematocytology:</u>		
Erythrocyte count	x	x
Packed cell volume	x	x
Hemoglobin	x	x
Leukocyte count	x	x
Differential leukocyte count	x	x
<u>Blood Biochemistry:</u>		
Glucose	x	x
BUN	x	x
SGOT	x	x
Alkaline phosphatase	x	x
SGPT	-	x
Sodium	-	x
Potassium	-	x
Chloride	-	x
<u>Urinalysis:</u>		
Color	x	x
Specific gravity	x	x
pH	x	x
Sugar	x	x
Protein (albumin)	x	x
Ketones (acetone)	x	x
Microscopic examination of sediment	x	x

3. EXPERIMENTAL DESIGN (Continued)

G. Terminations

All survivors were killed after 13 weeks. The planned 2 and 4 week recovery period was eliminated by agreement with the Project Officer since no effects had been seen.

H. Postmortem Examinations

Each animal was subjected to a gross necropsy and any observed abnormalities were recorded. The organs listed below were weighed.

heart	kidney	adrenals (after fixation)
liver	gonads	thyroid (after fixation)
spleen	brain	

Generous samples of each of the following were collected and held frozen for chemical analysis as indicators of tissue storage:

liver	brain	eye
kidneys	skeletal	testes
body fat	muscle	

Suitable samples of the following organs were preserved in 10% neutral formalin:

thyroid	small intestine	seminal vesicles
lung	large intestine	bone marrow
heart	kidneys	brain
mesenteric lymph node	adrenal glands	pituitary
liver	urinary bladder	thoracic spinal cord
spleen	testes with epididymis	rib junction
pancreas	or ovary	eye
stomach	uterus/prostate	nerve with muscle
		any unusual lesions

### 3. EXPERIMENTAL DESIGN (Continued)

#### I. Histopathologic Examination

The following tissues were examined microscopically from five male and five female rats in the control and high level test groups:

thyroid	small intestine	seminal vesicles
lung	large intestine	bone marrow
heart	kidneys	brain
mesenteric lymph	adrenal glands	pituitary
node	urinary bladder	thoracic spinal cord
liver	testes with epididymis	rib junction
spleen	or ovary	eye
pancreas	uterus/prostate	nerve with muscle
stomach		any unusual lesions

### 4. RESULTS

#### A. Drug Administration

No difficulty was encountered with the preparation of the diets according to plan or with their acceptance by the rats.

#### B. Observations

A total of 20/240 (8%) of the rats failed to survive to the planned sacrifice. Sixteen of these were males and 4 were females. They were essentially equally distributed among dosage groups. This mortality is judged to be unimportant. The average values for body weights are presented in Table II-D-38.

The occasional significant differences between control and treated groups are scattered and show no relationship to dosage or duration of treatment. They are judged to be of no toxicologic importance. Food consumption values are presented similarly in Table II-D-39. No important differences from controls were seen in either sex at any dosage. Other signs of toxicity were not noted.

#### C. Special Examinations

Ophthalmoscopic examinations during the week before termination reported all rats to be within normal limits.

#### 4. RESULTS (Continued)

##### D. Clinical Laboratory Measurements

The observed values for hematocytology at the four-week interval and at termination are presented in Table II-D-40. Only group means and standard errors are presented. Differential white cell counts are not analyzed statistically. The few instances of statistically significant differences from corresponding controls are so scattered as to be of no toxicologic importance.

The recorded values for various blood biochemistry measures at the four-week interval and at termination are tabulated in Table II-D-41. There are instances of statistically significant differences from control but they are judged to be of no toxicologic importance.

Urinalysis values obtained at four weeks and at termination are presented in Table II-D-42. No important deviations from normal were noted.

##### E. Postmortem Examination

The weights of various organs collected at terminal necropsy are presented in Table II-D-43 as recorded and in Table II-D-44 recalculated as percentages of body weight. The few indicated differences between groups in the original data disappear in the percentage tabulation.

##### G. Histopathological Examination

The tissues tested in 3I above were processed in the conventional manner for preparation of sections stained with hematoxylin and eosin for examination of a staff pathologist. The pathologist's own summary is attached. No important abnormalities were noted.

#### 5. CONCLUSIONS

No evidence of toxicity resulted from dietary administration of DCPD to rats at levels of 80, 250, and 750 ppm for 90 days.

90-DAY TOXICITY STUDY IN RATS

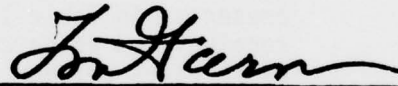
DCPD

LBI PROJECT NO. 2563

PATHOLOGY SUMMARY

The microscopic lesions observed in this study were those routinely encountered in rats and mice.

They appeared in all dosed groups and did not differ significantly from those seen in the controls.



F. M. Garner, D.V.M.

Veterinary Pathologist

Veterinary Sciences Division

TABLE 11-0-38

BODY WEIGHTS  
(kg)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

## MALES

## DCPD

CONTROL		12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	28	30	30	30	30	30	27	29	28	27	27	26	26	26	10	10	5	5
MEAN	87.1	136.6	181.4	226.1	291.1	318.0	318.0	314.1	305.3	292.1	303.0	309.8	329.5	333.9	330.7	341.2	337.7	339.5
S.E.	1.8	2.4	4.1	3.0	3.6	5.9	3.7	6.1	6.0	7.5	9.7	9.9	9.3	25.3	15.5	5.3	19.1	20.2

80 ppm		12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	30	28	30	30	29	29	29	29	28	10	10	5	5
MEAN	85.5	138.3	192.9	229.7	268.2	293.0	313.1	304.5	326.7	311.5	334.1	324.0	333.7	345.2	354.4	362.7	369.1	366.2
S.E.	2.1	2.0	2.0	3.3	3.4	5.5	6.4	6.0	6.8	5.9	6.1	8.0	10.3	26.6	17.4	6.8	29.5	33.3
T	0.6	0.5	2.5	0.8	0.4	0.2	0.6	1.1	2.4	2.1	2.8	1.1	0.3	0.5	1.0	1.5	0.9	0.7

250 ppm		12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	29	29	29	28	28	25	26	26	25	25	25	24	24	10	10	5	5
MEAN	86.8	141.2	187.5	220.5	261.1	286.0	305.5	314.5	321.2	320.6	326.1	325.5	329.5	345.4	360.4	368.7	372.9	394.7
S.E.	1.4	1.7	2.8	5.4	5.7	6.9	6.8	5.5	7.5	8.7	8.2	10.2	10.5	10.8	15.5	14.4	12.3	14.4
T	0.2	1.5	1.2	0.9	0.8	0.6	1.6	0.0	1.7	2.5	1.8	1.1	0.0	0.7	1.4	1.6	1.6	2.2

750 ppm		12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	30	28	30	29	27	28	27	27	27	9	9	4	4
MEAN	86.4	138.4	181.5	217.6	249.7	273.0	297.5	290.3	297.8	303.2	332.6	339.9	340.3	336.1	360.5	374.3	353.9	332.2
S.E.	1.6	2.2	3.0	4.1	5.8	7.4	8.9	10.1	13.4	6.7	8.8	8.8	8.1	32.9	12.4	29.9	19.7	2.9
T	0.3	0.5	0.0	1.7	2.4	1.9	3.0	2.0	0.5	1.1	2.6	2.5	0.9	0.1	1.5	2.2	0.6	0.5

TABLE II-D-38 (Continued)

BODY WEIGHTS  
(kg)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

## FEMALES

## DCPD

CONTROL		12/18	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	30	30	28	30	30	30	30	30	28	28	10	10	5	5
MEAN	75.3	111.9	144.6	161.3	177.2	188.2	192.1	200.7	192.1	205.0	193.1	200.1	200.5	214.9	218.1	223.1	225.1	232.1	231.9
S.E.	1.2	2.6	1.8	1.7	2.0	3.2	3.1	2.3	3.1	4.0	4.7	5.4	5.7	4.2	11.8	6.7	2.9	5.8	4.4
80 ppm		12/18	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	30	30	27	30	30	30	30	30	30	29	10	10	5	5
MEAN	75.1	117.3	146.9	158.9	178.8	191.6	192.0	200.1	202.1	208.8	203.4	214.5	216.1	218.6	220.7	222.9	229.2	227.8	228.3
S.E.	1.6	1.7	1.5	2.4	2.1	2.1	2.8	1.8	2.9	2.5	2.3	3.0	4.1	4.9	10.8	1.7	2.2	6.3	1.7
T	0.1	1.8	1.0	0.8	0.5	0.9	0.9	0.2	2.3	0.8	3.9	2.3	2.3	0.6	0.3	0.0	0.7	0.5	0.4
250 ppm		12/18	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	30	30	28	30	28	28	28	28	28	28	10	10	5	5
MEAN	74.7	118.2	147.0	162.0	180.0	192.0	192.0	195.0	192.9	223.1	195.1	218.8	212.0	219.2	220.8	231.4	235.8	259.1	235.7
S.E.	1.3	1.4	1.3	1.5	2.1	2.8	2.8	4.2	5.4	4.0	4.1	6.9	4.8	4.5	12.6	5.8	2.0	23.1	6.5
T	0.3	2.2	1.1	0.3	1.0	0.9	0.9	1.2	0.1	3.2	1.9	2.2	1.6	0.7	0.3	0.9	1.8	1.1	0.5
750 ppm		12/18	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	29	30	30	30	30	30	30	27	30	30	29	30	30	30	30	10	10	5	5
MEAN	74.4	117.4	144.6	161.5	175.9	185.1	195.1	195.9	200.6	205.4	205.1	210.5	212.2	208.3	219.0	221.6	227.4	221.4	224.0
S.E.	1.6	1.7	1.5	1.6	1.9	3.1	3.1	2.1	2.3	2.8	3.2	3.3	3.2	11.5	7.8	1.6	2.0	6.9	7.1
T	0.5	1.8	0.0	0.1	0.5	0.7	0.7	1.5	2.2	0.1	3.9	1.6	1.9	1.0	0.1	0.3	0.4	1.2	0.9

TABLE II-D-39

FOOD CONSUMPTION  
(Mean kg/day/rat)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

## MALES

## DCPD

CONTRL	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	27	29	28	27	26	25	25	25	10	10	5	5
MEAN	21.9	19.8	22.5	24.3	23.5	25.6	24.1	18.0	17.9	16.1	21.9	21.5	21.6	23.2	22.3	26.1	24.1
S.E.	0.4	0.3	0.3	0.4	0.4	0.6	0.7	0.9	0.8	0.9	0.8	2.0	0.8	1.2	0.4	2.6	2.0

80 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	29	30	27	30	30	25	29	28	28	27	9	8	5	5
MEAN	23.3	19.0	22.6	24.7	23.6	24.7	25.6	19.9	22.3	20.6	22.2	20.6	22.1	25.0	22.7	22.0	22.7
S.E.	0.5	0.4	0.5	0.4	0.7	0.6	0.8	1.0	0.8	0.6	3.2	3.8	0.8	0.3	0.5	1.8	2.2
t	2.2	2.0	0.2	0.8	0.1	0.2	1.4	1.5	3.7	2.2	0.2	0.4	0.4	1.6	0.4	1.3	0.5

250 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	29	29	28	27	28	25	26	26	22	12	25	24	23	10	7	4	5
MEAN	21.4	19.1	21.6	23.6	24.0	24.0	22.8	20.5	21.8	19.6	20.4	21.6	22.1	25.0	23.9	24.3	25.2
S.E.	0.8	0.7	0.6	0.4	0.7	0.7	0.8	1.1	0.9	2.1	2.6	1.2	0.9	0.7	0.6	0.5	1.5
t	0.6	1.1	1.3	1.1	0.6	0.7	1.2	1.9	3.0	0.9	0.9	0.1	0.4	1.1	1.7	0.7	0.4

750 ppm	12/25	1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	28	30	29	22	24	26	14	26	8	9	4	4
MEAN	20.8	17.0	21.1	22.0	22.3	22.9	21.4	20.8	24.3	20.8	22.4	19.1	19.7	24.2	24.0	21.0	19.5
S.E.	0.6	0.5	0.5	0.7	3.3	3.3	1.3	1.6	0.5	5.9	6.3	0.6	0.9	0.2	0.6	0.2	0.4
t	1.7	5.4	2.4	2.9	1.0	1.1	2.0	1.6	5.9	1.6	0.3	1.7	1.5	1.0	1.8	3.1	2.9

TABLE II-D-39 (Continued)

FOOD CONSUMPTION  
(mean kg/day/rat)

GROUP MEANS, STANDARD ERROR, STUDENT'S "t" TEST

FEMALES

DCPD

		1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
CONTRL 12/25		1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	28	30	30	29	27	30	26	26	10	10	5	5
MEAN	20.2	16.4	18.0	18.6	17.0	19.6	19.2	16.7	17.0	15.0	16.1	16.4	17.2	17.9	16.4	21.5	21.6
S.E.	0.8	0.6	1.7	0.5	0.6	0.7	1.7	0.9	0.7	0.7	0.7	0.5	0.4	0.4	3.0	0.5	2.0
80 ppm 12/25		1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	27	29	25	29	28	27	29	29	10	10	5	5
MEAN	19.9	15.3	16.7	18.4	17.1	17.9	19.0	16.5	17.7	17.0	15.6	15.9	17.0	18.7	15.9	15.3	17.1
S.E.	0.6	0.2	0.5	0.5	0.6	0.5	0.4	0.4	1.8	0.5	1.7	0.5	0.6	0.2	0.2	0.7	0.9
T	0.2	1.9	1.4	0.3	0.1	1.9	0.2	0.2	0.6	2.2	0.5	0.6	0.3	1.1	0.4	4.4	2.0
250 ppm 12/25		1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	30	30	26	30	25	24	25	22	27	25	9	10	5	5
MEAN	18.5	15.2	17.3	17.4	18.4	17.7	19.5	13.8	19.3	17.6	16.3	17.2	16.6	19.3	17.0	16.6	17.6
S.E.	0.4	0.2	1.5	0.5	0.8	0.5	3.2	1.0	0.7	0.9	0.6	0.6	0.5	0.2	0.4	0.4	1.1
T	1.9	2.0	0.5	1.8	1.5	2.0	0.4	2.2	2.3	2.1	0.2	1.0	0.9	1.9	0.4	3.6	1.7
750 ppm 12/25		1/1	1/8	1/15	1/22	1/29	2/5	2/12	2/19	2/26	3/4	3/11	3/18	3/25	4/1	4/8	4/15
WK NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SAMPLE	30	30	30	29	29	26	30	30	29	30	28	30	30	10	10	5	5
MEAN	19.6	15.2	18.1	17.2	18.2	17.4	17.8	16.9	17.0	16.2	15.2	16.3	16.7	19.2	17.2	18.8	20.1
S.E.	0.5	0.2	1.5	0.3	0.6	0.5	0.4	0.7	0.6	0.6	0.5	2.1	0.3	0.1	0.4	3.2	2.2
T	0.6	2.0	0.1	2.4	1.3	2.4	1.6	0.2	0.0	1.3	1.1	0.0	1.0	1.8	0.6	1.3	0.5

TABLE II-D-40  
HEMATOCYTOLOGY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm%</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	51.0	15.4	6.65	17.0
S.E.	0.82	0.40	0.15	1.5
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	51.5	15.9	6.68	13.4
S.E.	0.46	0.56	0.17	0.71
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.0	15.9	6.46	12.1
S.E.	0.51	0.43	0.17	0.98
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.0	15.1	6.59	12.4
S.E.	0.93	0.43	0.10	1.2

TABLE II-D-40 (Continued)

HEMATOCYTOLOGY

GROUP MEANS AND STANDARD ERROR

13 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm%</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	53.0	17.2	7.78	17.0
S.E.	2.6	0.84	0.55	1.8
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.9	6.62	13.7
S.E.	1.2	0.35	0.22	0.70
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	52.5	17.2	7.85	12.5
S.E.	0.85	0.23	0.19	1.2
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	53.5	17.7	7.91	13.3
S.E.	1.6	0.57	0.13	1.8

TABLE II-D-40 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS AND STANDARD ERROR

4 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm%</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	51.0	16.0	6.67	10.9
S.E.	0.74	0.34	0.15	0.68
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	48.0	15.4	6.23	9.3
S.E.	0.62	0.35	0.16	0.78
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.0	15.8	6.57	10.7
S.E.	1.0	0.20	0.12	0.71
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	15.5	6.30	10.0
S.E.	0.87	0.55	0.052	0.72

TABLE II-D-40 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>CELL VOL. %</u>	<u>HEMO- GLOBIN gm%</u>	<u>RBC/mm<sup>3</sup> (x 10<sup>6</sup>)</u>	<u>WBC/mm<sup>3</sup> (x 10<sup>3</sup>)</u>
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	52.5	17.3	7.82	14.5
S.E.	1.6	0.58	0.44	2.0
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	49.0	16.7	7.19	11.2
S.E.	2.3	0.70	0.29	1.3
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.8	6.81	9.2
S.E.	1.2	0.40	0.071	1.4
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	50.5	16.8	7.16	10.3
S.E.	0.84	0.25	0.20	1.7

TABLE II-D-41  
BLOOD CHEMISTRY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg %	<u>GLU- COSE</u> mg %	<u>ALK. PHOS.</u> I.U.	<u>SGPT</u> I.U.
<u>MALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	5	5
MEAN	16	68	183	17
S.E.	1.3	19	17	1.5
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	15	83	144	15
S.E.	1.2	7.9	14	1.2
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	16	64	161	16
S.E.	1.6	12	11	2.4
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	15	79	159	15
S.E.	1.9	5.5	8.5	2.3

TABLE II-D-41 (Continued)

## BLOOD CHEMISTRY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg%	<u>GLU- COSE</u> mg%	<u>ALK. PHOS.</u> I.U.	<u>SGOT</u> I.U.	<u>SGPT</u> I.U.	<u>Cl</u> mEq/L	<u>K</u> mEq/L	<u>Na</u> mEq/L
<u>MALES</u>								
<u>1 - CONTROL</u>								
NO. SAMPLES	5	5	5	5	5	3	4	1
MEAN	22	80	122	304	43	177	8.8	212
S.E.	1.3	11	40	51	18	1.5	0.42	
<u>2 - 80 ppm</u>								
NO. SAMPLES	5	5	5	5	5	4	5	1
MEAN	18	76	114	253	28	178	9.1	209
S.E.	0.71	6.5	6.8	19	4.9	1.7	0.58	
<u>3 - 250 ppm</u>								
NO. SAMPLES	5	5	5	5	5	2	3	1
MEAN	16	80	88	260	24	176	9.1	205
S.E.	0.75	8.2	4.7	19	0.84	1.5	0.24	
<u>4 - 750 ppm</u>								
NO. SAMPLES	5	5	5	5	5	4	5	1
MEAN	20	75	75	266	28	175	9.9	195
S.E.	1.1	7.7	16	26	3.4	2.5	0.95	

TABLE II-D-41 (Continued)

BLOOD CHEMISTRY  
GROUP MEANS AND STANDARD ERROR  
4 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg %	<u>GLU- COSE</u> mg %	<u>ALK. PHOS.</u> I.U.	<u>SGPT</u> I.U.
<u>FEMALES</u>				
<u>1 - CONTROL</u>				
NO. SAMPLES	5	5	4	5
MEAN	17	89	141	18
S.E.	1.8	10	29	4.5
<u>2 - 80 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	16	80	119	14
S.E.	1.4	6.2	8.4	1.5
<u>3 - 250 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	18	77	119	12
S.E.	0.92	11	9.0	1.3
<u>4 - 750 ppm</u>				
NO. SAMPLES	5	5	5	5
MEAN	20	79	121	13
S.E.	2.6	6.1	12	1.6

TABLE II-D-41 (Continued)

## BLOOD CHEMISTRY

## GROUP MEANS AND STANDARD ERROR

13 WEEKS - DCPD

<u>GROUP NO. &amp; DOSAGE LEVEL</u>	<u>BUN</u> mg%	<u>GLU- COSE</u> mg%	<u>ALK. PHOS.</u> I.U.	<u>SGOT</u> I.U.	<u>SGPT</u> I.U.	<u>Cl</u> mEq/L	<u>K</u> mEq/L	<u>Na</u> mEq/L
<u>FEMALES</u>								
<u>1 - Control</u>								
NO. SAMPLES	5	5	5	5	5	4	5	1
MEAN	21	84	91	247	20	175	8.4	191
S.E.	1.9	11	15	16	2.1	1.1	0.44	
<u>2 - 80 ppm</u>								
NO. SAMPLES	5	5	5	5	5	3	5	2
MEAN	17	95	72	261	22	173	8.7	207
S.E.	0.40	8.6	12	14	1.6	1.2	0.43	5.5
<u>3 - 250 ppm</u>								
NO. SAMPLES	5	5	5	5	5	3	5	2
MEAN	20	97	97	272	19	176	8.1	201
S.E.	0.73	11	13	8.1	0.98	2.2	0.35	8.0
<u>4 - 750 ppm</u>								
NO. SAMPLES	5	5	5	5	5	4	5	1
MEAN	22	84	92	256	19	172	7.6	197
S.E.	1.9	8.7	11	5.9	1.3	1.4	0.25	

TABLE II-D-42

URINALYSIS

KEY

Color: Y = Yellow  
Or = Orange  
Br = Brown  
Str = Straw

Casts: fgr = Finely Granular

Crystals: T.P. = Triple Phosphate  
U.A. = Uric Acid  
Ca O = Calcium Oxalate

- or 0 = None or Negative  
+ = Trace, Occasional, Rare,  
Very Little  
1+ = Slight, Small, Little,  
Few, Some, Light  
2+ = Moderate, Frequent, Large  
3+ = Severe, Heavy, Many  
4+ = Maximal  
TNTC = Too Numerous to Count

TABLE II-D-42

## URINALYSIS

4 WEEKS - DCPD - MALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL- BUMIN	GLU- COSE	KE- TONES	BILI- RUBIN	OCCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*																									
										GROUP 1 - CONTROL					GROUP 2 - 80 ppm					GROUP 3 - 250 ppm					GROUP 4 - 750 ppm										
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	T.P.	CA.	OX	OTHER	WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	T.P.	CA.	OX	OTHER	WBC	RBC	EPITH	CASTS
10992	Br	Turbid	1.026	9	1+	0	0	0	1+	-	25-30	-	-	3+	4+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10993	Str	Cloudy	1.007	7	0	0	0	0	0	4-8	-	-	-	2+	4+	-	2+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10994	Y	Clear	1.032	6	+	0	0	0	0	2-3	1-2	-	-	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10995	Y	Hazy	1.028	7	2+	0	0	0	1+	4-8	0-3	0-1	-	1+	1+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10996	Y	Clear	1.021	7	+	0	0	0	0	1-2	0-1	3-4	-	-	1+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
GROUP 2 - 80 ppm																																			
11056	Str	Cloudy	1.007	9	0	0	0	0	0	2-5	-	0-3	-	2+	4+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11057	Y	Clear	1.035	7	0	0	0	0	0	1-2	0-1	1-2	-	-	2+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11059	Str	Cloudy	1.013	9	2+	0	0	0	0	0-1	-	2-5	-	-	4+	-	4+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11060	Y	Clear	1.018	7	1+	0	0	0	0	4-5	1-2	1-2	-	-	1+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
GROUP 3 - 250 ppm																																			
11121	Br	Turbid	1.031	9	2+	0	0	0	1+	-	-	-	-	4+	4+	-	4+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11123	Y	Hazy	1.029	7	2+	0	0	0	2+	15-20	TNTC	4-8	-	-	4+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11124	Y	Cloudy	1.013	9	2+	0	0	0	1+	10-15	-	0-1	-	2+	4+	-	4+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11125	Y	Clear	1.024	6	1+	0	0	0	0	2-3	4-5	-	-	-	1+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
GROUP 4 - 750 ppm																																			
11184	Br	Turbid	1.032	9	1+	0	0	0	+	-	-	-	-	4+	4+	-	4+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11187	Y	Cloudy	1.025	9	3+	0	0	0	1+	10-15	-	4-8	-	1+	4+	-	3+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11188	Y	Clear	1.028	7	2+	0	0	0	0	3-4	2-3	1-2	-	-	-	-	2+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

\* Microscopic examination per high power field.

TABLE II-D-42 (Continued)

## URINALYSIS

13 WEEKS - DCPD - MALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	BILI-RUBIN	OCCULT BLOOD	MBC	RBC	MICROSCOPIC EXAMINATION/HPF*						
												EPITH	CASTS	AMORPH	BACT.	CRYSTALS		
																U.A.	T.P.	CA.OX
GROUP 1 - CONTROL																		
111004	Y	Clear	1.043	5	2+	0	1+	0	0	0-1	-	0-3	-	1+	3+	-	-	-
111005	Y	Hazy	1.090	5	4+	0	2+	0	0	0-1	0-3	0-1	-	-	1+	-	2+	-
111006	Y	Hazy	1.090	5	4+	0	2+	0	0	2-5	0-3	2-5	-	1+	2+	-	3+	-
111007	Y	Hazy	1.010	8	0	0	0	0	0	0-1	-	-	-	1+	4+	-	3+	-
111008	Y	Hazy	1.070	6	4+	0	2+	0	0	4-8	4-8	-	-	1+	4+	-	3+	-
GROUP 2 - 80 ppm																		
111068	Y	Hazy	1.040	6	3+	0	1+	0	0	0-1	-	0-3	-	1+	4+	-	3+	-
111070	Y	Clear	1.029	6	4+	0	1+	0	0	-	-	0-1	-	-	3+	-	2+	-
111071	Y	Cloudy	1.029	9	0	0	0	0	0	-	-	-	-	-	4+	-	4+	-
111072	Y	Cloudy	1.024	8	2+	0	0	0	0	0-1	-	-	-	1+	4+	-	3+	-
111073	Y	Cloudy	1.040	8	2+	0	1+	0	0	4-8	TNTC	-	-	3+	4+	-	4+	-
GROUP 3 - 250 ppm																		
111135	Y	Hazy	1.090	5	4+	0	2+	0	0	0-1	0-1	0-1	-	1+	2+	-	3+	-
111137	Or	Hazy	1.045	6	4+	0	2+	0	0	-	-	-	-	-	4+	-	2+	-
111139	Or	Hazy	1.095	6	4+	0	2+	0	0	-	-	-	-	2+	2+	-	3+	-
111140	Y	Hazy	1.014	8	3+	0	0	0	0	-	-	-	-	-	4+	-	4+	-
111142	Y	Hazy	1.090	6	4+	0	1+	0	0	0-1	-	0-1	-	1+	4+	-	-	-
GROUP 4 - 750 ppm																		
111197	Y	Clear	1.045	6	2+	0	1+	0	0	0-1	10-15	0-1	-	-	-	-	3+	-
111198	Or	Hazy	1.043	7	3+	0	1+	0	0	0-1	20-25	-	-	-	4+	-	2+	-
111199	Or	Cloudy	1.038	9	1+	0	1+	0	0	0-1	-	-	-	2+	4+	-	3+	-
111200	Or	Hazy	1.075	6	4+	0	1+	0	0	0-1	2-5	0-3	-	1+	2+	-	2+	-

\* Microscopic examination per high power field.

TABLE II-D-42 (Continued)

## URINALYSIS

4 WEEKS - DCPD - FEMALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	BILI-RUBIN	OCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*									
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	CRYSTALS			
																U.A.	T.P.	CA.OX	OTHER
GROUP 1 - CONTROL																			
111024	Or	Cloudy	1.035	9	1+	0	0	0	1+	0-3	20-25	-	-	1+	4+	-	3+	-	-
111026	Y	Clear	1.030	5	2+	0	0	0	0	4-5	-	-	-	-	3+	-	1+	-	-
111027	Y	Hazy	1.040	6	1+	0	0	0	+	0-1	-	0-1	-	-	1+	-	-	-	-
111028	Y	Clear	1.026	6	0	0	0	0	0	2-3	2-3	-	-	-	2+	-	1+	-	-
GROUP 2 - 80 ppm																			
111088	Y	Cloudy	1.026	9	0	0	0	0	0	TNTC	-	0-1	-	4+	4+	-	4+	-	-
111089	Y	Clear	1.030	6	0	0	0	0	0	1-2	1-2	1-2	-	-	1+	-	1+	-	-
111090	Str	Cloudy	1.013	7	2+	0	0	0	0	0-3	-	2-5	-	1+	4+	-	-	-	-
111091	Y	Clear	1.022	5	0	0	0	0	0	2-3	1-2	-	-	-	2+	-	-	-	-
111092	Y	Clear	1.027	5	+	0	0	0	0	3-4	0-1	0-1	-	-	-	-	-	-	-
GROUP 3 - 250 ppm																			
111152	Br	Turbid	1.024	9	1+	0	0	0	+	-	-	-	-	3+	4+	-	3+	-	-
111154	Y	Cloudy	1.024	9	1+	0	0	0	0	0-3	-	0-2	-	3+	4+	-	3+	-	-
111155	Y	Clear	1.016	6	0	0	0	0	0	4-5	2-3	-	-	-	1+	-	-	-	-
GROUP 4 - 750 ppm																			
11216	Br	Turbid	1.021	9	0	0	0	0	+	-	-	-	-	4+	4+	-	4+	-	-
11217	Br	Turbid	1.019	9	1+	0	0	0	1+	-	-	-	-	4+	4+	-	4+	-	-
11218	Y	Clear	1.021	7	0	0	0	0	0	2-3	0-1	-	-	-	3+	-	1+	-	-
11219	Y	Cloudy	1.028	8	1+	0	0	0	0	20-25	-	0-1	-	2+	4+	3+	4+	-	-
11220	Y	Clear	1.018	7	0	0	0	0	0	1-2	1-2	-	-	-	+	-	-	-	-

\* Microscopic examination per high power field.

TABLE II-D-42 (Continued)

## URINALYSIS

13 WEEKS - DCPD - FEMALES

RAT NO.	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL- BUMIN	GLU- COSE	KE- TONES	BILI- RUBIN	OCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*								CRYSTALS			
										WBC	RBC	EPITH	CASTS	AMORPH	BACT.	U.A.	T.P.	CA.OX	OTHER		
GROUP 1 - CONTROL																					
11034	Y	Hazy	1.033	6	0	0	0	0	0	0-2	-	0-1	-	1+	4+	-	2+	-	-		
11036	Y	Clear	1.038	6	0	0	0	0	0	0-1	-	0-1	-	-	-	-	1+	-	-		
11038	Y	Cloudy	1.021	8	0	0	0	0	0	0-1	-	0-1	-	2+	4+	-	3+	-	-		
11039	Y	Hazy	1.040	5	4+	0	2+	0	0	0-1	-	0-3	-	2+	-	-	-	-	-		
11040	Y	Hazy	1.095	6	3+	0	1+	0	0	0-1	-	4-8	-	-	4+	-	3+	-	-		
GROUP 2 - 80 ppm																					
11098	Y	Hazy	1.070	5	4+	0	2+	0	0	-	-	0-1	-	2+	2+	-	-	-	-		
11099	Y	Hazy	1.040	6	4+	0	1+	0	0	0-1	-	0-1	-	-	3+	-	3+	-	-		
11100	Y	Cloudy	1.020	9	1+	0	0	0	0	-	-	-	-	3+	4+	-	3+	-	-		
11101	Y	Hazy	1.095	6	4+	0	1+	0	0	0-1	10-15	4-8	-	1+	4+	-	2+	-	-		
11103	Y	Cloudy	1.045	6	1+	0	0	0	0	0-1	-	0-1	-	-	4+	-	-	-	-		
GROUP 3 - 250 ppm																					
11163	Y	Hazy	1.090	5	4+	0	2+	0	0	0-1	10-15	0-1	-	2+	3+	-	-	-	-		
11164	Or	Hazy	1.080	6	4+	0	1+	0	0	-	-	-	-	-	1+	-	3+	-	-		
11165	Y	Hazy	1.013	7	0	0	0	0	0	0-1	-	0-3	-	2+	4+	-	-	-	-		
11167	Y	Hazy	1.090	6	3+	0	1+	0	0	-	-	-	-	3+	3+	-	3+	-	-		
GROUP 4 - 750 ppm																					
11226	Y	Cloudy	1.060	5	3+	0	1+	0	0	4-8	0-1	0-1	-	0-1	2+	-	-	3+	-		
11227	Y	Hazy	1.028	6	0	0	1+	0	0	0-3	-	0-3	-	-	4+	-	3+	-	-		
11228	Y	Hazy	1.021	6	0	0	0	0	0	-	-	0-2	-	1+	4+	-	-	-	-		
11229	Y	Hazy	1.023	6	1+	0	0	0	0	0-3	-	-	-	-	4+	-	1+	-	-		
11230	Y	Hazy	1.090	5	2+	0	1+	0	0	0-1	-	0-1	-	1+	-	-	-	-	-		

\* Microscopic examination per high power field.

TABLE II-D-43

ORGAN WEIGHTS IN MALE RATS  
(grams)

## GROUP 1 - CONTROL

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
10992	339.1	1.5480	0.0	1.2120	13.9940	0.7090	3.4690	0.0580	4.9590
10993	440.4	1.8010	0.0220	1.6520	18.3000	0.8190	3.9210	0.0550	5.2800
10994	339.0	1.6990	0.0200	1.2150	12.7630	0.7210	2.9590	0.0460	5.5690
10996	290.4	1.6870	0.0150	1.0330	12.9900	0.7510	2.7250	0.0510	4.3700
10997	370.8	1.6440	0.0210	1.3370	19.8520	0.6520	4.0080	0.0600	5.8280
10998	388.9	1.9220	0.0280	1.4930	18.1900	0.0	3.4900	0.0590	6.0800
10999	270.0	1.5930	0.0260	1.1630	9.6570	0.5120	2.5430	0.0550	3.4300
11000	389.0	1.8640	0.0200	1.3120	15.0210	0.5750	3.5000	0.0480	5.1880
11001	318.5	1.7620	0.0200	1.3390	13.7830	0.5950	3.3080	0.0590	4.9680
11003	332.0	1.6700	0.0190	1.2270	15.4430	0.5980	2.8950	0.0700	2.9980
11004	357.3	1.7450	0.0220	1.2500	17.1500	0.7090	3.2710	0.0590	4.7640
11005	334.5	0.0	0.0140	1.4790	16.6570	0.7360	3.3120	0.0620	5.2570
11006	393.9	1.7770	0.0340	1.4360	17.7580	0.7510	3.6170	0.0650	4.7090
11007	393.3	1.6180	0.0220	1.3290	15.2820	0.6420	3.1690	0.0	4.4710
11008	350.0	1.6420	0.0170	1.0520	11.4620	0.4890	2.8520	0.0340	4.7750
11009	292.0	1.7230	0.0100	1.0370	12.2000	0.4380	2.7300	0.0	3.7290
11010	363.1	1.6440	0.0180	1.3090	14.6500	0.6670	3.0820	0.0430	4.8540
11011	359.4	1.6650	0.0150	1.4600	18.8980	0.6460	3.2100	0.0450	4.6200
11013	340.1	1.7290	0.0250	1.2390	15.1200	0.7260	3.4400	0.0570	5.2290
11016	435.2	1.7780	0.0250	1.6770	18.2830	0.7150	4.1470	0.0640	5.2070
11017	337.6	1.6290	0.0190	1.3870	16.7020	0.8040	3.2920	0.0580	4.1090
11018	279.4	1.6950	0.0160	1.4570	16.2050	0.5270	2.7380	0.0490	3.5890
11019	354.0	1.7390	0.0220	1.2310	17.4610	0.6570	3.0630	0.0470	4.6230
11020	364.5	1.7130	0.0120	1.3510	18.2750	0.7130	3.4230	0.0540	4.9350
11022	382.3	1.7890	0.0230	1.2500	18.6920	0.7780	3.3290	0.0520	4.8640
11023	332.0	1.5200	0.0150	1.1280	15.6280	0.6440	2.7970	0.0640	4.8880
N	26	25	25	26	26	25	26	24	26
MEAN	351.8	1.7038	0.0200	1.3098	15.7852	0.6630	3.2419	0.0548	4.7420
S.D.	42.4	0.0925	0.0053	0.1673	2.5732	0.0990	0.4082	0.0083	0.7157
S.E.	8.3	0.0185	0.0011	0.0328	0.5046	0.0198	0.0801	0.0017	0.1404

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 2 - 80 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11056	374.8	1.7590	0.0240	1.2520	14.4490	0.6440	3.1150	0.0590	5.3530
11058	255.0	1.3180	0.0240	0.8060	7.4890	0.5040	2.2720	0.0440	4.1920
11059	420.2	1.8660	0.0250	1.6910	18.4760	0.7190	3.6890	0.0900	5.1030
11060	337.6	1.6310	0.0220	1.3940	18.6350	0.6870	3.3990	0.0820	4.8090
11061	414.8	1.8830	0.0300	1.4430	17.3100	0.6140	4.0010	0.0	4.7180
11063	381.0	1.7420	0.0260	1.4460	16.0440	0.6540	3.6310	0.0440	5.2210
11064	374.0	0.0	0.0230	1.2870	13.5460	0.6370	3.2020	0.0520	5.2480
11066	405.5	1.9000	0.0160	1.3900	18.1500	0.0	3.9500	0.0520	5.3780
11067	436.0	1.7920	0.0290	1.4910	15.2760	0.7250	3.8360	0.0570	5.2600
11068	346.0	1.7530	0.0350	1.0990	13.2240	0.6840	3.0650	0.0630	4.5170
11070	375.0	1.6770	0.0280	1.3530	16.0830	0.7310	3.5190	0.0630	4.6580
11071	366.2	1.8480	0.0190	1.2070	13.7830	0.6690	3.3480	0.0580	5.1210
11072	375.0	1.7900	0.0270	1.1500	15.8220	0.7820	3.5090	0.0570	4.8950
11073	372.0	1.7100	0.0230	1.4110	18.5870	0.5170	3.5470	0.0640	5.2290
11074	380.0	1.5920	0.0200	1.1450	14.8450	0.5880	3.4150	0.0570	5.0530
11075	385.0	1.6890	0.0280	1.2220	19.2090	0.6670	3.7530	0.0770	4.8880
11076	401.5	1.5390	0.0210	0.9780	10.5250	0.4860	2.4310	0.0550	4.1150
11077	342.3	1.7020	0.0190	1.2600	15.8950	0.6850	3.2590	0.0500	4.9900
11078	366.1	1.2060	0.0150	1.2590	15.3940	0.6460	3.6010	0.0530	3.8000
11079	389.0	1.5910	0.0330	1.1470	16.8710	0.6980	3.3700	0.0540	4.8650
11080	356.5	1.7460	0.0290	1.2710	15.6450	0.7520	3.3680	0.0590	5.0070
11081	422.0	1.6430	0.0350	1.5740	22.7690	0.6480	3.8770	0.0640	5.2070
11082	347.1	1.6710	0.0170	1.5150	17.7380	0.5090	2.9640	0.0	4.9200
11083	380.7	1.7430	0.0220	1.4230	15.9440	0.6980	3.5010	0.0440	4.8020
11084	265.8	1.6360	0.0200	1.3980	15.8130	0.7450	2.6360	0.0550	3.1070
11086	398.3	1.9180	0.0180	1.2940	15.4780	0.7320	3.6840	0.0600	5.3970
11087	360.2	1.6680	0.0200	1.2040	17.5040	0.6320	3.3610	0.0500	4.7630
N	27	26	27	27	27	26	27	25	27
MEAN	371.4	1.7005	0.0240	1.3004	15.9446	0.6559	3.3816	0.0590	4.8376
S.D.	40.6	0.1634	0.0056	0.1858	2.8713	0.0800	0.4277	0.0104	0.5220
S.E.	7.8	0.0320	0.0011	0.0358	0.5526	0.0157	0.0823	0.0021	0.1005

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 3 - 250 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
11122	380.6	1.7980	0.0250	1.5490	16.5210	0.6420	3.4470	0.0600	4.8550
11123	331.0	1.7150	0.0140	1.5290	17.0350	0.6440	2.9970	0.0740	5.0480
11124	344.4	1.6940	0.0330	1.1370	16.5320	0.6140	3.2130	0.0750	5.0980
11125	293.7	1.7890	0.0170	1.1470	4.7580	0.5800	3.3540	0.0600	4.3410
11126	325.6	1.6650	0.0340	1.1350	15.4620	0.7540	3.1600	0.0570	4.6900
11128	358.0	1.7930	0.0300	1.3000	13.3040	0.7340	3.4790	0.0590	5.1210
11129	397.0	1.7900	0.0210	1.4640	14.8030	0.8350	3.5660	0.0660	5.2420
11130	438.8	1.7720	0.0270	1.3970	16.3520	0.7370	3.6270	0.0770	5.5770
11133	395.0	0.0	0.0200	1.3850	14.7550	0.8770	3.5070	0.0660	5.2140
11134	400.3	1.6560	0.0230	1.3490	15.7950	0.6200	3.7520	0.0560	5.3780
11135	416.4	1.6820	0.0180	1.4880	21.0910	0.7240	3.9880	0.0470	5.0600
11137	331.3	1.7160	0.0320	1.2370	12.8510	0.9030	3.2110	0.0800	4.8420
11139	325.4	1.6250	0.0330	1.1080	12.8100	0.6200	2.9580	0.0530	4.8790
11140	340.5	1.5940	0.0240	1.2030	13.0000	0.7230	3.2690	0.0540	4.8140
11141	202.0	1.6430	0.0370	0.8840	8.5340	0.3980	2.1950	0.0680	3.3580
11142	347.6	1.8390	0.0310	1.1470	16.6720	0.6990	3.5960	0.0630	4.9700
11143	315.5	1.7120	0.0	1.2540	12.6550	0.7720	3.0130	0.0	3.6830
11144	384.0	1.6250	0.0290	1.2420	16.3160	0.8620	3.5710	0.0640	4.6040
11145	414.0	1.6850	0.0240	1.3730	20.0630	0.6870	3.9550	0.0710	4.8770
11146	423.0	1.7320	0.0290	1.2880	18.4750	0.7340	3.8770	0.0700	5.2670
11148	344.5	1.6510	0.0270	1.6920	16.9130	0.5820	3.5200	0.0780	5.1810
11150	407.4	1.6530	0.0300	1.3770	15.8670	0.7100	3.5760	0.0680	5.1720
11151	385.4	1.7870	0.0240	1.6230	19.8290	0.5690	3.4100	0.0580	4.6540
N	23	22	22	23	23	23	23	22	23
MEAN	361.1	1.7098	0.0266	1.3177	15.2345	0.6965	3.4018	0.0647	4.8663
S.D.	52.5	0.0690	0.0057	0.1892	3.6048	0.1155	0.3887	0.0089	0.5082
S.E.	10.9	0.0147	0.0012	0.0394	0.7516	0.0241	0.0811	0.0014	0.1060

TABLE II-D-43 (Continued)

ORGAN WEIGHTS IN MALE RATS  
(grams)

GROUP 4 - 750 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11184	273.0	1.7290	0.0180	0.9890	9.7740	0.7390	2.6120	0.0	3.8270
11185	274.0	1.7090	0.0310	1.2390	9.1590	0.5600	2.7880	0.0510	3.5980
11186	358.0	1.7720	0.0240	1.3320	13.0870	0.5710	3.2390	0.0	4.9720
11188	410.4	1.7520	0.0240	1.3130	14.8600	0.8300	3.6730	0.0590	5.2720
11189	412.8	1.4690	0.0210	1.3890	16.3070	0.7220	3.4030	0.0540	5.8220
11190	397.3	1.6150	0.0	1.5070	15.7910	0.8070	3.6810	0.0530	5.3400
11191	359.9	1.7590	0.0260	1.5130	13.5080	0.5400	3.4450	0.0610	4.9140
11193	369.6	1.7250	0.0210	1.2380	16.2230	0.6450	3.8300	0.0490	4.6060
11194	380.6	1.4290	0.0240	1.5090	14.7970	0.6180	3.9630	0.0	5.1380
11197	284.0	1.5690	0.0270	0.9900	14.2540	0.6360	2.9000	0.0540	4.2260
11198	302.1	1.7370	0.0160	1.1410	12.0400	0.7350	3.2820	0.0440	3.8200
11199	265.4	1.6630	0.0220	0.9900	8.1210	0.5430	2.6230	0.0770	3.5210
11200	335.0	1.3950	0.0280	1.1500	15.0310	0.6090	3.3290	0.0440	4.7910
11201	368.4	1.6420	0.0230	1.2510	17.5420	0.6410	4.1670	0.0640	5.4690
11202	383.0	1.5650	0.0240	1.1750	16.2540	0.6150	3.5270	0.0670	4.7010
11204	304.0	1.6580	0.0180	0.9050	12.1690	0.7750	3.0010	0.0530	4.1280
11205	378.0	1.6880	0.0200	1.1710	14.9670	0.5290	3.4270	0.0570	4.9180
11206	334.0	1.5740	0.0270	1.1240	15.2700	0.6790	3.4140	0.0600	4.6910
11207	300.0	1.6790	0.0190	1.4540	14.8770	0.5430	3.0400	0.0640	5.0430
11208	357.0	1.6470	0.0210	1.3350	13.9930	0.6370	3.1860	0.0590	4.7870
11209	428.0	1.7050	0.0	1.1820	20.7900	0.6670	4.1410	0.0540	4.8960
11210	399.0	1.6540	0.0210	1.1190	17.8480	0.6850	4.0280	0.0600	5.4640
11211	422.6	1.6240	0.0230	1.2510	19.9710	0.7570	3.9340	0.0630	5.1590
11212	344.0	1.7250	0.0240	1.0660	16.8960	0.6090	2.7620	0.0530	4.7220
11213	212.0	1.8830	0.0230	1.0140	8.8960	0.3020	2.4470	0.0750	2.2180
11214	372.6	1.6950	0.0180	1.0960	19.1100	0.6550	3.8090	0.0	4.8800
N	26	26	24	26	26	26	26	22	26
MEAN	347.3	1.6562	0.0226	1.2093	14.6744	0.6403	3.3712	0.0549	4.6509
S.D.	55.4	0.1086	0.0036	0.1727	3.2639	0.1087	0.4972	0.0079	0.7680
S.E.	10.9	0.0213	0.0007	0.0339	0.6401	0.0213	0.0975	0.0017	0.1506

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 1 - CONTROL

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11024	134.8	1.6370	0.0280	1.0820	4.0210	0.1980	1.3910	0.0810	0.1050
11025	241.0	1.5730	0.0230	0.9060	8.1090	0.4330	1.9670	0.0690	0.1100
11026	235.0	1.5360	0.0150	0.9610	8.7990	0.4440	2.0740	0.0670	0.1220
11027	242.1	1.7980	0.0170	0.8690	10.2990	0.4930	2.3800	0.0780	0.2190
11028	233.1	1.7370	0.0130	0.8440	9.0790	0.4590	2.0780	0.0660	0.0580
11029	251.1	1.6400	0.0200	1.3240	9.9700	0.4940	2.1920	0.0	0.1140
11030	250.4	1.7560	0.0200	0.8040	9.6240	0.5660	2.1160	0.0700	0.0940
11031	213.0	1.6080	0.0180	0.9060	7.9040	0.4940	1.5800	0.0560	0.0950
11032	228.0	1.6440	0.0170	0.9050	8.1560	0.4280	2.0410	0.0580	0.1110
11033	240.0	1.8820	0.0	1.0220	10.4900	0.5890	2.3690	0.0930	0.1420
11034	238.2	1.6990	0.0210	0.9360	10.9150	0.6470	2.1140	0.0650	0.1100
11035	201.3	1.5680	0.0200	0.7390	8.0740	0.5210	1.8160	0.0620	0.0950
11036	220.8	1.4970	0.0300	0.8610	7.8990	0.5840	2.0140	0.0950	0.0810
11038	243.0	1.5850	0.0320	0.8390	10.5140	0.4650	1.9280	0.0810	0.1670
11039	186.5	1.6200	0.0170	0.9190	7.2470	0.4630	1.8140	0.0690	0.0830
11040	245.0	1.5310	0.0130	0.9680	9.1660	0.5780	2.2550	0.0550	0.1410
11041	205.0	1.4580	0.0200	0.7680	11.8040	0.4580	2.1300	0.0740	0.1180
11043	217.0	1.5250	0.0200	0.7270	9.1350	0.5130	2.0190	0.0800	0.1080
11044	262.4	1.6250	0.0240	0.9180	8.8610	0.5910	2.2260	0.0680	0.1750
11045	223.1	1.6440	0.0240	0.8970	8.8510	0.5430	2.0190	0.0720	0.1260
11046	220.1	1.5880	0.0170	0.8240	10.9870	0.9420	1.9010	0.0640	0.0860
11047	228.4	1.7380	0.0190	1.1940	10.6100	0.5220	1.9320	0.0650	0.1120
11048	235.8	1.6650	0.0300	0.7880	8.2650	0.4320	2.0430	0.0710	0.0610
11049	246.6	1.6850	0.0240	0.9050	8.7780	0.6350	2.1180	0.0720	0.1190
11050	195.0	1.4340	0.0210	0.8370	7.8810	0.4220	1.6830	0.0	0.1160
11051	259.1	1.6490	0.0210	1.0660	11.2620	0.6580	2.3760	0.0820	0.1280
11052	221.7	1.5490	0.0150	0.8140	7.8900	0.4880	1.9860	0.0	0.0800
11053	245.1	1.5230	0.0120	0.8950	9.2750	0.4850	2.1970	0.0	0.0990
N	28	28	27	28	28	28	28	24	28
MEAN	227.2	1.6212	0.0204	0.9114	9.0666	0.5195	2.0271	0.0723	0.1134
S.D.	26.1	0.1024	0.0052	0.1320	1.5696	0.1228	0.2280	0.0112	0.0339
S.E.	4.9	0.0194	0.0010	0.0249	0.2966	0.0232	0.0431	0.0023	0.0064

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 2 - 80 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11088	249.7	1.5920	0.0170	0.8910	9.7920	0.5340	2.1070	0.0800	0.1400
11089	239.4	1.5890	0.0350	0.9780	10.5070	0.5280	2.1900	0.0930	0.1330
11090	246.0	1.4810	0.0130	0.8830	8.7500	0.4830	1.9790	0.0	0.1320
11091	187.4	1.5200	0.0130	0.9620	7.9730	0.4540	2.0430	0.0	0.1350
11092	243.0	1.6210	0.0250	0.8580	8.3700	0.4590	2.0970	0.0820	0.1320
11093	230.0	1.6320	0.0230	0.8650	8.7760	0.3980	2.0510	0.0770	0.1280
11094	217.0	1.6020	0.0	0.8660	8.4250	0.4950	1.9760	0.0640	0.0830
11095	214.7	1.6210	0.0160	0.7530	7.9910	0.4470	1.8710	0.0820	0.0890
11096	250.0	1.5980	0.0210	0.9010	9.4880	0.4250	2.3060	0.0	0.1500
11097	228.0	1.5990	0.0240	0.8660	8.7670	0.5010	1.9920	0.0660	0.1470
11098	226.1	1.7560	0.0170	0.8500	8.9150	0.6350	1.9920	0.0760	0.0830
11099	236.0	1.5330	0.0200	0.8820	9.6380	0.4820	1.9990	0.0550	0.1110
11100	242.0	1.7000	0.0400	0.8460	10.3890	0.8170	2.0750	0.0440	0.1490
11101	221.3	1.6450	0.0140	0.8670	9.6100	0.5710	1.9230	0.0680	0.0710
11103	227.4	1.6450	0.0220	0.8440	10.0050	0.5820	1.9140	0.0910	0.1050
11104	241.0	1.3550	0.0210	0.8610	9.7810	0.5390	2.1790	0.0930	0.1470
11105	249.0	1.7340	0.0220	0.8780	10.8300	0.4620	2.0870	0.0	0.0700
11106	221.1	1.2570	0.0120	1.0040	10.1370	0.4640	2.0010	0.0690	0.0690
11107	239.8	1.2540	0.0170	0.8890	9.7630	0.4190	1.9940	0.0690	0.0820
11108	190.4	1.5940	0.0260	0.7130	6.9740	0.4780	1.7950	0.0540	0.1130
11109	230.0	1.6250	0.0140	0.8370	9.1410	0.5360	1.9760	0.0850	0.0870
11110	244.9	1.4590	0.0270	1.0390	9.4040	0.5320	2.0080	0.0310	0.0910
11111	198.2	1.3990	0.0310	0.8310	8.3770	0.5480	1.9260	0.0580	0.1220
11113	249.3	1.6720	0.0200	0.8560	9.2310	0.5720	2.1920	0.0930	0.0620
11114	252.4	1.5890	0.0140	0.8780	8.3480	0.5430	2.0880	0.0550	0.0920
11115	226.1	1.2570	0.0140	0.8460	9.9320	0.5720	2.0050	0.0600	0.1160
11116	227.5	1.4420	0.0100	0.8880	9.6600	0.4490	1.8930	0.0640	0.0500
11118	248.0	1.3100	0.0100	0.9550	10.8030	0.5180	1.9990	0.0640	0.1670
11119	220.9	1.4140	0.0120	0.6810	7.4380	0.3710	1.6910	0.0670	0.0500
N	29	29	29	29	29	29	29	29	29
MEAN	230.9	1.5343	0.0202	0.8713	9.2143	0.5108	2.0120	0.0737	0.1071
S.D.	17.5	0.1443	0.0071	0.0746	0.9725	0.0845	0.1235	0.0123	0.0331
S.E.	3.2	0.0268	0.0014	0.0138	0.1806	0.0157	0.0229	0.0025	0.0061

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 3 - 250 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11152	253.2	1.7380	0.0200	0.8170	8.4600	0.5160	1.9370	0.0970	0.1550
11153	237.9	1.6950	0.0210	1.0090	10.2830	0.5270	2.0580	0.0740	0.0930
11154	262.4	1.2360	0.0210	0.9010	9.2620	0.5520	2.2670	0.0940	0.1840
11155	219.6	1.5400	0.0220	0.9230	9.1260	0.5370	2.0470	0.0720	0.1460
11156	196.0	1.4930	0.0160	0.8230	6.9420	0.4400	1.7760	0.0690	0.1360
11157	250.0	1.7310	0.0240	1.0060	8.8730	0.5460	2.1450	0.0760	0.1430
11158	235.0	1.7610	0.0210	0.9150	7.9790	0.5430	1.9250	0.0740	0.1290
11159	237.0	1.6250	0.0170	0.8250	8.4890	0.4570	1.8360	0.0640	0.1460
11161	218.0	1.6290	0.0230	0.8320	7.5540	0.5190	1.8210	0.0740	0.1420
11162	248.0	1.6580	0.0170	0.9840	8.3930	0.5000	1.8340	0.0720	0.1010
11163	211.6	1.5660	0.0140	0.7840	9.3250	0.5630	1.9130	0.0720	0.0930
11164	245.8	1.5720	0.0220	0.9400	9.3000	0.7230	1.9750	0.0720	0.1170
11165	242.0	0.0	0.0140	0.7980	8.2790	0.5230	1.8150	0.0670	0.1410
11166	232.1	1.4410	0.0250	0.8400	8.3120	0.5470	1.9600	0.0750	0.1110
11167	264.0	1.4860	0.0170	0.9340	9.8980	0.6030	2.3190	0.0660	0.1220
11168	224.4	1.6740	0.0150	0.8370	7.3250	0.4350	1.9990	0.0620	0.1080
11169	206.0	1.3970	0.0270	0.7350	8.6730	0.4260	2.0160	0.0640	0.1130
11170	217.0	1.4160	0.0190	0.7650	8.0990	0.3880	2.2420	0.0760	0.0920
11171	216.5	1.6440	0.0190	0.8730	10.0500	0.5510	1.9580	0.0	0.0910
1117	244.3	1.6530	0.0190	0.8960	8.7740	0.4620	2.2130	0.0	0.1030
11173	206.0	1.4630	0.0280	0.7240	7.1670	0.3780	1.6250	0.0700	0.0650
11174	215.3	1.7190	0.0190	0.8440	8.7540	0.4530	1.9630	0.0710	0.0840
11175	243.7	1.6280	0.0170	0.8420	10.1780	0.5300	2.1150	0.0740	0.0840
11176	175.9	1.6070	0.0170	0.7770	6.2140	0.4220	1.5100	0.0600	0.1100
11177	178.5	1.4520	0.0180	0.8070	6.6950	0.4670	1.7980	0.0600	0.0420
11179	254.0	1.5260	0.0210	0.8640	11.0670	0.5820	2.3490	0.0630	0.1820
11180	245.2	1.5540	0.0170	1.0490	10.7400	0.5570	2.4010	0.0	0.1010
11181	273.2	1.7990	0.0200	1.3990	11.1140	0.6110	2.3350	0.0410	0.1200
N	28	27	28	28	28	28	28	28	28
MEAN	230.4	1.5834	0.0194	0.8438	8.7616	0.5128	2.0054	0.0725	0.1162
S.D.	24.4	0.1291	0.0034	0.1306	1.2906	0.0748	0.2216	0.0040	0.0323
S.E.	4.6	0.0248	0.0006	0.0247	0.2439	0.0141	0.0419	0.0014	0.0061

TABLE II-D-43 (Continued)  
ORGAN WEIGHTS IN FEMALE RATS  
(grams)

GROUP 4 - 750 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11216	249.8	1.7300	0.0260	0.8970	8.5860	0.5890	2.1600	0.0750	0.1070
11217	246.0	1.5950	0.0190	0.8800	7.8090	0.5090	1.9140	0.0770	0.1360
11218	217.5	1.5720	0.0210	0.9520	7.8240	0.4300	1.8320	0.0710	0.1380
11219	238.6	0.0	0.0190	0.0940	7.8250	0.4650	0.2900	0.0680	0.1490
11220	215.0	1.4910	0.0250	0.7980	7.8410	0.6360	1.7200	0.0790	0.1740
11221	213.0	1.5400	0.0200	0.8430	7.6580	0.4430	1.7780	0.0610	0.1110
11222	237.0	1.6700	0.0220	1.0320	8.6140	0.6360	2.0330	0.0930	0.1410
11223	240.2	1.6940	0.0280	0.9250	8.0230	0.5730	2.1790	0.0920	0.1270
11224	205.9	1.7340	0.0170	0.8100	8.8060	0.3690	1.7860	0.0670	0.1750
11225	210.9	1.5640	0.0200	0.8720	7.6220	0.4980	1.9880	0.0700	0.1430
11226	246.0	1.5630	0.0170	0.7680	9.4500	0.4460	2.2220	0.0830	0.1330
11227	245.8	1.6110	0.0260	0.8850	8.2650	0.5120	2.2630	0.0730	0.0800
11228	228.7	1.7180	0.0200	0.8460	8.5000	0.4420	2.0670	0.0800	0.1300
11229	209.0	1.6830	0.0110	0.8850	8.1540	0.4670	1.5620	0.0700	0.1210
11230	217.6	1.5660	0.0200	0.7700	8.5600	0.6000	1.8600	0.0600	0.1640
11231	233.4	1.5040	0.0200	1.1710	10.3780	0.4490	2.0460	0.0630	0.1100
11232	250.4	1.7050	0.0220	0.8290	10.0790	0.4110	2.2500	0.0740	0.0790
11233	229.0	1.6020	0.0120	0.8260	8.4010	0.4360	1.8690	0.0650	0.1030
11234	231.1	1.6780	0.0260	0.8890	8.6560	0.5120	2.0890	0.0650	0.1540
11235	227.0	1.5260	0.0210	0.7710	8.6690	0.4520	2.0370	0.0590	0.1380
11236	244.0	1.5530	0.0190	0.7940	9.2680	0.4340	2.0220	0.0740	0.1500
11237	255.0	1.6770	0.0170	0.8170	9.6240	0.5770	2.0170	0.0670	0.1230
11238	251.3	1.7980	0.0130	1.0760	9.6740	0.5850	2.1410	0.0740	0.0970
11240	222.5	1.4730	0.0260	0.9560	9.3110	0.4860	1.8940	0.0530	0.1060
11241	257.3	1.3990	0.0230	1.0600	10.7460	0.5040	2.1910	0.0820	0.0920
11242	232.0	1.1330	0.0230	0.9910	8.2220	0.4440	1.6570	0.0790	0.1990
11243	242.0	1.6350	0.0150	1.0710	1.8930	0.5990	1.9990	0.0840	0.1400
11244	241.0	1.7130	0.0180	0.9180	10.8890	0.4250	2.0720	0.0810	0.1300
11245	236.2	1.4040	0.0240	0.8700	8.0800	0.5990	1.8580	0.0740	0.0390
11246	228.1	1.5120	0.0200	1.0090	10.4130	0.5990	2.0480	0.0720	0.0240
N	30	29	30	30	30	30	30	30	30
MEAN	233.4	1.5877	0.0205	0.8768	8.5947	0.5042	1.9281	0.0732	0.1238
S.D.	14.5	0.1335	0.0045	0.1804	1.5838	0.0758	0.3560	0.0003	0.0274

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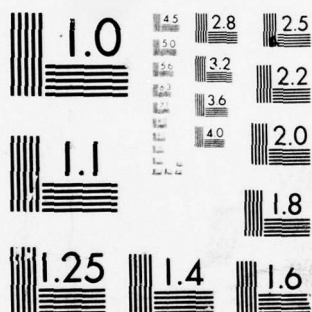
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MICROCOPY RESOLUTION TEST CHART  
NATIONAL BUREAU OF STANDARDS-1963-A

TABLE II-D-44

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

## GROUP 1 - CONTROL

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
10992	0.4565	0.0	0.3574	4.1268	0.2091	1.0230	0.0171	1.4624
10993	0.4089	0.0050	0.3751	4.1553	0.1860	0.8903	0.0125	1.1989
10994	0.5012	0.0059	0.3584	3.7649	0.2127	0.8729	0.0136	1.6428
10996	0.5809	0.0052	0.3557	4.4731	0.2586	0.9384	0.0176	1.5048
10997	0.4434	0.0057	0.3606	5.3538	0.1758	1.0809	0.0162	1.5717
10998	0.4942	0.0072	0.3839	4.6773	0.0	0.8974	0.0152	1.5634
10999	0.5900	0.0096	0.4307	3.5767	0.1896	0.9419	0.0204	1.2704
11000	0.4792	0.0051	0.3373	3.8614	0.1478	0.8997	0.0123	1.3337
11001	0.5532	0.0063	0.4204	4.3275	0.1868	1.0386	0.0185	1.5598
11003	0.5030	0.0057	0.3696	4.6515	0.1801	0.8720	0.0211	0.9030
11004	0.4884	0.0062	0.3498	4.7999	0.1984	0.9155	0.0165	1.3333
11005	0.0	0.0042	0.4422	4.9797	0.2200	0.9901	0.0185	1.5716
11006	0.4511	0.0086	0.3646	4.5083	0.1907	0.9183	0.0165	1.1955
11007	0.4114	0.0056	0.3379	3.8856	0.1632	0.8057	0.0	1.1368
11008	0.4691	0.0049	0.3006	3.2749	0.1397	0.8149	0.0097	1.3643
11009	0.5901	0.0034	0.3551	4.1781	0.1500	0.9349	0.0	1.2771
11010	0.4528	0.0050	0.3605	4.0347	0.1837	0.8488	0.0118	1.3368
11011	0.4633	0.0042	0.4062	5.2582	0.1797	0.8932	0.0125	1.2855
11013	0.5084	0.0074	0.3643	4.4457	0.2135	1.0115	0.0168	1.5375
11016	0.4085	0.0057	0.3853	4.2011	0.1643	0.9529	0.0147	1.1965
11017	0.4825	0.0056	0.4108	4.9473	0.2382	0.9751	0.0172	1.2171
11018	0.6067	0.0057	0.5215	5.7999	0.1886	0.9800	0.0175	1.2845
11019	0.4912	0.0062	0.3477	4.9325	0.1856	0.8653	0.0133	1.3059
11020	0.4700	0.0033	0.3706	5.0137	0.1956	0.9391	0.0148	1.3539
11022	0.4680	0.0060	0.3270	4.8894	0.2035	0.8708	0.0136	1.2723
11023	0.4578	0.0045	0.3398	4.7072	0.1940	0.8425	0.0193	1.4723
N	25	25	26	26	25	26	24	26
MEAN	0.4892	0.0057	0.3744	4.4932	0.1902	0.9236	0.0157	1.3520
S.D.	0.0560	0.0014	0.0442	0.5863	0.0270	0.0694	0.0029	0.1700
S.E.	0.0112	0.0003	0.0087	0.1150	0.0054	0.0136	0.0006	0.0333

TABLE II-D-44 (ContinueJ)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 2 - 80 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
11056	0.4693	0.0064	0.3340	3.8551	0.1718	0.8311	0.0157	1.4282
11058	0.5169	0.0094	0.3161	2.9369	0.1976	0.8910	0.0188	1.6439
11059	0.4441	0.0059	0.4024	4.3970	0.1711	0.8779	0.0214	1.2144
11060	0.4831	0.0065	0.4129	5.5198	0.2035	1.0068	0.0243	1.4245
11061	0.4540	0.0072	0.3479	4.1731	0.1480	0.9646	0.0	1.1374
11063	0.4572	0.0068	0.3795	4.2110	0.1717	0.9530	0.0129	1.3703
11064	0.0	0.0061	0.3441	3.6219	0.1703	0.8561	0.0139	1.4032
11066	0.4686	0.0039	0.3428	4.4760	0.0	0.9741	0.0128	1.3263
11067	0.4110	0.0067	0.3420	3.5037	0.1663	0.8798	0.0131	1.2064
11068	0.5066	0.0101	0.3176	3.8220	0.1977	0.8858	0.0182	1.3055
11070	0.4472	0.0075	0.3608	4.2888	0.1949	0.9384	0.0168	1.2421
11071	0.5046	0.0052	0.3296	3.7638	0.1827	0.9143	0.0158	1.3984
11072	0.4773	0.0072	0.3067	4.2192	0.2085	0.9357	0.0152	1.3053
11073	0.4597	0.0062	0.3793	4.9965	0.1390	0.9535	0.0172	1.4056
11074	0.4189	0.0053	0.3013	3.9066	0.1547	0.8987	0.0150	1.3297
11075	0.4387	0.0073	0.3174	4.9893	0.1732	0.9748	0.0200	1.2696
11076	0.3833	0.0052	0.2436	2.6214	0.1210	0.6055	0.0137	1.0249
11077	0.4972	0.0056	0.3681	4.6436	0.2001	0.9521	0.0146	1.4578
11078	0.3294	0.0041	0.3439	4.2049	0.1765	0.9836	0.0145	1.0380
11079	0.4090	0.0085	0.2949	4.3370	0.1794	0.8663	0.0139	1.2506
11080	0.4898	0.0081	0.3565	4.3885	0.2109	0.9447	0.0165	1.4045
11081	0.3893	0.0085	0.3730	5.3955	0.1536	0.9187	0.0152	1.2339
11082	0.4814	0.0049	0.4355	5.1103	0.1466	0.8539	0.0	1.4175
11083	0.4578	0.0058	0.3738	4.1881	0.1833	0.9196	0.0126	1.2614
11084	0.6907	0.0075	0.5260	5.9492	0.2803	0.9917	0.0207	1.1689
11086	0.4815	0.0045	0.3249	3.8860	0.1838	0.9249	0.0151	1.3550
11087	0.4631	0.0056	0.3343	4.8595	0.1755	0.9331	0.0139	1.3223
N	26	27	27	27	26	27	25	27
MEAN	0.4627	0.0055	0.3522	4.3061	0.1793	0.9122	0.0161	1.3091
S.D.	0.0633	0.0015	0.0526	0.7433	0.0302	0.0764	0.0030	0.1324
S.E.	0.0124	0.0003	0.0101	0.1431	0.0059	0.0147	0.0006	0.0255

TABLE II-D-44 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS

GROUP 3 - 250 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11122	0.4724	0.0066	0.4070	4.3408	0.1687	0.9057	0.0158	1.2756
11123	0.5181	0.0054	0.4619	5.1465	0.1946	0.9054	0.0224	1.5251
11124	0.4919	0.0096	0.3301	4.8002	0.1783	0.9329	0.0218	1.4803
11125	0.6091	0.0058	0.3905	1.6200	0.1975	1.1420	0.0204	1.4780
11126	0.5114	0.0104	0.3486	4.7488	0.2316	0.9705	0.0175	1.4404
11128	0.5008	0.0084	0.3631	3.7162	0.2050	0.9718	0.0165	1.4304
11129	0.4509	0.0053	0.3638	3.7287	0.2103	0.8982	0.0166	1.3204
11130	0.4038	0.0062	0.3184	3.7265	0.1680	0.8266	0.0175	1.2710
11133	0.0	0.0051	0.3506	3.7354	0.2220	0.8878	0.0167	1.3200
11134	0.4137	0.0057	0.3370	3.9458	0.1549	0.9373	0.0140	1.3435
11135	0.4039	0.0043	0.3573	5.0651	0.1739	0.9577	0.0113	1.2152
11137	0.5180	0.0097	0.3734	3.8790	0.2726	0.9692	0.0241	1.4615
11139	0.4994	0.0101	0.3405	3.9367	0.1905	0.9090	0.0163	1.4994
11140	0.4681	0.0070	0.3533	3.8179	0.2123	0.9601	0.0159	1.4138
11141	0.8134	0.0183	0.4376	4.2248	0.1970	1.0866	0.0337	1.6624
11142	0.5291	0.0049	0.3300	4.7963	0.2011	1.0345	0.0181	1.4298
11143	0.5426	0.0	0.3975	4.0111	0.2447	0.9550	0.0	1.1674
11144	0.4232	0.0076	0.3234	4.2490	0.2245	0.9299	0.0167	1.1990
11145	0.4070	0.0059	0.3316	4.8461	0.1659	0.9553	0.0171	1.1780
11146	0.4095	0.0069	0.3045	4.3676	0.1735	0.9165	0.0165	1.2452
11148	0.4724	0.0077	0.4841	4.8392	0.1665	1.0072	0.0223	1.4824
11150	0.4057	0.0074	0.3380	3.8947	0.1743	0.8778	0.0167	1.2695
11151	0.4637	0.0062	0.4211	5.1450	0.1476	0.8848	0.0150	1.2076
N	22	22	23	23	23	23	22	23
MEAN	0.4876	0.0077	0.3682	4.1992	0.1946	0.9488	0.0183	1.3616
S.D.	0.0910	0.0030	0.0473	0.7536	0.0307	0.0695	0.0045	0.1333
S.E.	0.0194	0.0006	0.0099	0.1571	0.0064	0.0145	0.0010	0.0278

TABLE II-D-44 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE RATS  
GROUP 4 - 750 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
11184	0.6333	0.0066	0.3623	3.5802	0.2707	0.9568	0.0	1.4018
11185	0.6237	0.0113	0.4522	3.3427	0.2044	1.0175	0.0186	1.3131
11186	0.4950	0.0067	0.3721	3.6556	0.1595	0.9047	0.0	1.3888
11188	0.4269	0.0058	0.3199	3.6209	0.2022	0.8950	0.0144	1.2846
11189	0.3559	0.0051	0.3365	3.9503	0.1749	0.8244	0.0141	1.4104
11190	0.4065	0.0	0.3793	3.9746	0.2031	0.9265	0.0133	1.3441
11191	0.4887	0.0072	0.4204	3.7533	0.1500	0.9572	0.0169	1.3654
11193	0.4667	0.0057	0.3350	4.3893	0.1745	1.0363	0.0133	1.2462
11194	0.3755	0.0063	0.3965	3.8878	0.1624	1.0413	0.0	1.3500
11197	0.5448	0.0094	0.3437	4.9493	0.2208	1.0069	0.0187	1.4674
11198	0.5750	0.0053	0.3777	3.9854	0.2433	1.0864	0.0159	1.2645
11199	0.6266	0.0083	0.3730	3.0599	0.2046	0.9883	0.0290	1.3267
11200	0.4164	0.0084	0.3433	4.4869	0.1818	0.9937	0.0143	1.4301
11201	0.4457	0.0062	0.3396	4.7617	0.1740	1.1311	0.0174	1.4845
11202	0.4086	0.0063	0.3068	4.2439	0.1606	0.9209	0.0175	1.2274
11204	0.5454	0.0059	0.2977	4.0030	0.2549	0.9872	0.0174	1.3579
11205	0.4466	0.0053	0.3098	3.9595	0.1399	0.9066	0.0151	1.3011
11206	0.4713	0.0081	0.3365	4.5719	0.2033	1.0222	0.0180	1.4045
11207	0.5597	0.0063	0.4847	4.9590	0.1810	1.0133	0.0227	1.6810
11208	0.4613	0.0059	0.3739	3.9196	0.1784	0.8924	0.0165	1.3409
11209	0.3944	0.0	0.2762	4.8575	0.1558	0.9675	0.0136	1.1439
11210	0.4145	0.0053	0.2805	4.4732	0.1717	1.0095	0.0150	1.3694
11211	0.3843	0.0054	0.2960	4.7257	0.1791	0.9309	0.0149	1.2208
11212	0.5015	0.0070	0.3099	4.9116	0.1770	0.8029	0.0154	1.3727
11213	0.8842	0.0104	0.4783	4.1962	0.1425	1.1542	0.0354	1.0462
11214	0.4549	0.0044	0.2941	5.1288	0.1758	1.0223	0.0	1.3097
N	26	24	26	26	26	26	22	26
MEAN	0.4929	0.0084	0.3537	4.2057	0.1864	0.9768	0.0176	1.3405
S.D.	0.1131	0.0017	0.0569	0.5494	0.0329	0.0826	0.0053	0.1187
S.F.	0.0222	0.0004	0.0112	0.1077	0.0064	0.0162	0.0011	0.0233

TABLE II-D-44 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 1 - CONTROL

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11024	1.2144	0.0204	0.8027	2.9829	0.1469	1.0319	0.0601	0.0779
11025	0.6527	0.0045	0.3759	3.3647	0.1797	0.8162	0.0286	0.0456
11026	0.6536	0.0064	0.4089	3.7443	0.1889	0.8826	0.0285	0.0519
11027	0.7427	0.0070	0.3589	4.2540	0.2036	0.9831	0.0322	0.0905
11028	0.7452	0.0056	0.3621	3.8949	0.1969	0.8915	0.0283	0.0249
11029	0.6531	0.0080	0.5273	3.9705	0.1967	0.8730	0.0	0.0454
11030	0.7013	0.0080	0.3211	3.8434	0.2260	0.8450	0.0280	0.0375
11031	0.7549	0.0045	0.4254	3.7108	0.2319	0.7418	0.0263	0.0446
11032	0.7211	0.0075	0.3969	3.5772	0.1877	0.8952	0.0254	0.0487
11033	0.7842	0.0	0.4258	4.3708	0.2454	0.9871	0.0387	0.0592
11034	0.7133	0.0088	0.3929	4.5823	0.2716	0.8875	0.0273	0.0462
11035	0.7789	0.0061	0.3671	4.0109	0.2588	0.9021	0.0281	0.0472
11036	0.6780	0.0161	0.3899	3.5774	0.2645	0.9121	0.0509	0.0367
11038	0.6523	0.0131	0.3453	4.3267	0.1914	0.7934	0.0331	0.0687
11039	0.8686	0.0083	0.4928	3.8858	0.2483	0.9727	0.0337	0.0445
11040	0.6249	0.0060	0.3951	3.7412	0.2359	0.9204	0.0253	0.0576
11041	0.7112	0.0076	0.3746	5.7580	0.2234	1.0390	0.0297	0.0576
11043	0.7028	0.0090	0.3350	4.2097	0.2364	0.9304	0.0349	0.0498
11044	0.6193	0.0109	0.3498	3.3769	0.2252	0.8483	0.0300	0.0667
11045	0.7369	0.0097	0.4021	3.9673	0.2434	0.9050	0.0373	0.0565
11046	0.7215	0.0087	0.3744	4.9918	0.4280	0.8637	0.0328	0.0391
11047	0.7609	0.0073	0.5228	4.6454	0.2285	0.8459	0.0251	0.0490
11048	0.7061	0.0135	0.3342	3.5051	0.1832	0.8664	0.0320	0.0259
11049	0.6833	0.0114	0.3670	3.5596	0.2575	0.8589	0.0358	0.0483
11050	0.7354	0.0086	0.4292	4.0415	0.2164	0.8631	0.0	0.0595
11051	0.6364	0.0062	0.4114	4.3466	0.2540	0.9170	0.0349	0.0494
11052	0.6987	0.0064	0.3672	3.5589	0.2201	0.8958	0.0	0.0361
11053	0.6214	0.0049	0.3652	3.7842	0.1979	0.8964	0.0	0.0404
N	28	27	28	28	28	28	24	28
MEAN	0.7240	0.0043	0.4079	3.9851	0.2282	0.8952	0.0320	0.0502
S.D.	0.1117	0.0044	0.0928	0.5587	0.0494	0.0657	0.0081	0.0142
S.E.	0.0211	0.0007	0.0175	0.1056	0.0093	0.0124	0.0017	0.0027

TABLE II-D-44 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS  
GROUP 2 - 80 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
11088	0.6376	0.0068	0.3568	3.9215	0.2139	0.8438	0.0320	0.0561
11089	0.6637	0.0146	0.4085	4.3889	0.2206	0.9148	0.0388	0.0556
11090	0.6020	0.0073	0.3589	3.5569	0.1963	0.8045	0.0	0.0537
11091	0.8111	0.0101	0.5133	4.2545	0.2423	1.0902	0.0	0.0720
11092	0.6671	0.0103	0.3531	3.4444	0.1889	0.8630	0.0337	0.0543
11093	0.7096	0.0100	0.3761	3.8157	0.1730	0.8917	0.0335	0.0557
11094	0.7382	0.0	0.3991	3.8825	0.2281	0.9106	0.0313	0.0382
11095	0.7550	0.0075	0.3507	3.7219	0.2082	0.8714	0.0382	0.0415
11096	0.6392	0.0044	0.3604	3.7952	0.1700	0.9224	0.0	0.0600
11097	0.7013	0.0105	0.3798	3.8452	0.2197	0.8737	0.0289	0.0645
11098	0.7766	0.0075	0.3759	3.9429	0.2808	0.8810	0.0336	0.0367
11099	0.6496	0.0085	0.3737	4.0839	0.2042	0.8470	0.0233	0.0470
11100	0.7025	0.0165	0.3496	4.2930	0.3376	0.8574	0.0347	0.0616
11101	0.7433	0.0053	0.3918	4.3425	0.2580	0.8690	0.0307	0.0321
11103	0.7234	0.0097	0.3712	4.3997	0.2559	0.8417	0.0400	0.0462
11104	0.5622	0.0087	0.3573	4.0585	0.2237	0.9041	0.0386	0.0610
11105	0.6964	0.0088	0.3526	4.3494	0.1855	0.8382	0.0	0.0281
11106	0.5685	0.0054	0.4541	4.5848	0.2099	0.9050	0.0312	0.0312
11107	0.5229	0.0071	0.3707	4.0713	0.1747	0.8315	0.0288	0.0342
11108	0.8372	0.0137	0.3745	3.6628	0.2511	0.9428	0.0305	0.0593
11109	0.7065	0.0078	0.3639	3.9743	0.2330	0.8591	0.0370	0.0378
11110	0.5958	0.0110	0.4243	3.8399	0.2172	0.8199	0.0331	0.0372
11111	0.7059	0.0156	0.4193	4.2265	0.2765	0.9717	0.0293	0.0616
11113	0.6707	0.0080	0.3434	3.7028	0.2294	0.8793	0.0373	0.0249
11114	0.6296	0.0055	0.3479	3.3074	0.2151	0.8273	0.0218	0.0365
11115	0.5559	0.0062	0.3742	4.3927	0.2530	0.8868	0.0265	0.0513
11116	0.6338	0.0044	0.3903	4.2462	0.1974	0.8321	0.0281	0.0220
11118	0.5282	0.0040	0.3851	4.3560	0.2089	0.8060	0.0274	0.0673
11119	0.6401	0.0054	0.3083	3.3671	0.1679	0.7655	0.0303	0.0226
N	29	29	29	29	29	29	29	29
MEAN	0.6681	0.0084	0.3788	3.9941	0.2221	0.8742	0.0320	0.0466
S.D.	0.0800	0.0032	0.0384	0.3414	0.0376	0.0607	0.0048	0.0144
S.E.	0.0149	0.0006	0.0071	0.0634	0.0070	0.0113	0.0010	0.0027

TABLE II-D-44 (Continued)  
ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 3 - 250 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11152	0.6864	0.0079	0.3227	3.3412	0.2038	0.7650	0.0383	0.0612
11153	0.7125	0.0088	0.4241	4.3224	0.2215	0.8651	0.0328	0.0391
11154	0.4710	0.0080	0.3434	3.5297	0.2104	0.8639	0.0358	0.0701
11155	0.7013	0.0100	0.4203	4.1557	0.2445	0.9321	0.0328	0.0665
11156	0.7617	0.0082	0.4199	3.5418	0.2245	0.9061	0.0352	0.0694
11157	0.6924	0.0096	0.4024	3.5492	0.2184	0.8580	0.0304	0.0572
11158	0.7494	0.0089	0.3894	3.3953	0.2311	0.8191	0.0315	0.0549
11159	0.6857	0.0072	0.3481	3.5819	0.1928	0.7747	0.0287	0.0616
11161	0.7472	0.0093	0.3817	3.4651	0.2381	0.8353	0.0298	0.0651
11162	0.6685	0.0078	0.3968	3.3843	0.2016	0.7395	0.0330	0.0407
11163	0.7401	0.0085	0.3705	4.4069	0.2661	0.9041	0.0340	0.0440
11164	0.6395	0.0090	0.3824	3.7836	0.2941	0.8035	0.0293	0.0476
11165	0.0	0.0058	0.3298	3.4211	0.2161	0.7500	0.0277	0.0583
11166	0.6381	0.0108	0.3619	3.5812	0.2357	0.8445	0.0323	0.0478
11167	0.5629	0.0064	0.3538	3.7492	0.2284	0.8784	0.0250	0.0462
11168	0.7460	0.0067	0.3730	3.2643	0.1939	0.8908	0.0276	0.0481
11169	0.6782	0.0131	0.3568	4.2102	0.2068	0.9786	0.0311	0.0549
11170	0.6525	0.0088	0.3525	3.7323	0.1788	1.0332	0.0350	0.0424
11171	0.7612	0.0083	0.4032	4.6420	0.2545	0.9044	0.0	0.0420
1117	0.6766	0.0073	0.3668	3.5915	0.1891	0.9059	0.0	0.0422
11173	0.7102	0.0136	0.3515	3.4791	0.1835	0.7888	0.0340	0.0316
11174	0.7944	0.0088	0.3939	4.0660	0.2104	0.9118	0.0330	0.0390
11175	0.6630	0.0070	0.3455	4.1764	0.2175	0.8679	0.0324	0.0345
11176	0.4136	0.0097	0.4417	3.5327	0.2399	0.8584	0.0341	0.0625
11177	0.8134	0.0101	0.4521	3.7507	0.2616	1.0073	0.0336	0.0235
11179	0.6008	0.0083	0.3402	4.3571	0.2291	0.9248	0.0248	0.0717
11180	0.6354	0.0069	0.4278	4.3801	0.2272	0.9792	0.0	0.0412
11181	0.6585	0.0073	0.5121	4.0681	0.2236	0.8547	0.0295	0.0439
N	27	28	28	28	28	28	28	28
MEAN	0.6952	0.0087	0.3844	3.8021	0.2230	0.8730	0.0317	0.0503
S.D.	0.0841	0.0018	0.0428	0.3940	0.0263	0.0747	0.0033	0.0126
S.E.	0.0162	0.0003	0.0081	0.0745	0.0050	0.0141	0.0007	0.0024

TABLE II-D-44 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE RATS

GROUP 4 - 750 ppm

DCPD

ANIMAL NUMBER	BRAIN	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
11216	0.6926	0.0104	0.3591	3.4371	0.2358	0.8647	0.0300	0.0428
11217	0.6484	0.0077	0.3577	3.1744	0.2069	0.7780	0.0313	0.0553
11218	0.7228	0.0097	0.4377	3.5972	0.1977	0.8423	0.0326	0.0634
11219	0.0	0.0080	0.0394	3.2795	0.1949	0.1215	0.0285	0.0624
11220	0.6935	0.0116	0.3712	3.6470	0.2958	0.8000	0.0367	0.0809
11221	0.7230	0.0094	0.3958	3.5953	0.2080	0.8347	0.0286	0.0521
11222	0.7046	0.0093	0.4354	3.6346	0.2684	0.8578	0.0392	0.0595
11223	0.7052	0.0117	0.3851	3.3401	0.2386	0.9072	0.0383	0.0529
11224	0.8422	0.0083	0.3934	4.2768	0.1792	0.8674	0.0325	0.0850
11225	0.7416	0.0095	0.4135	3.6140	0.2361	0.9426	0.0332	0.0678
11226	0.6354	0.0069	0.3122	3.8415	0.1813	0.9033	0.0337	0.0541
11227	0.6554	0.0106	0.3600	3.3625	0.2083	0.9207	0.0297	0.0325
11228	0.7512	0.0087	0.3699	3.7167	0.1933	0.9038	0.0350	0.0568
11229	0.8053	0.0053	0.4234	3.9014	0.2234	0.7474	0.0335	0.0579
11230	0.7197	0.0092	0.3539	3.9338	0.2757	0.8548	0.0276	0.0754
11231	0.6444	0.0086	0.5017	4.4464	0.1924	0.8766	0.0270	0.0471
11232	0.6809	0.0088	0.3311	4.0252	0.1641	0.8986	0.0296	0.0315
11233	0.6996	0.0052	0.3607	3.6686	0.1904	0.8162	0.0284	0.0450
11234	0.7261	0.0113	0.3847	3.7456	0.2215	0.9039	0.0299	0.0666
11235	0.6722	0.0093	0.3396	3.8189	0.1991	0.8974	0.0260	0.0608
11236	0.6365	0.0078	0.3254	3.7984	0.1779	0.8287	0.0320	0.0615
11237	0.6576	0.0067	0.3204	3.7741	0.2263	0.7910	0.0263	0.0482
11238	0.7155	0.0052	0.4282	3.8496	0.2328	0.8520	0.0310	0.0386
11240	0.6620	0.0117	0.4297	4.1847	0.2184	0.8512	0.0238	0.0476
11241	0.5437	0.0089	0.4120	4.1764	0.1959	0.8515	0.0319	0.0358
11242	0.4884	0.0099	0.4272	3.5440	0.1914	0.7142	0.0341	0.0858
11243	0.6756	0.0062	0.4426	0.7822	0.2475	0.8260	0.0347	0.0579
11244	0.7108	0.0075	0.3809	4.5183	0.1763	0.8598	0.0336	0.0539
11245	0.5944	0.0123	0.3683	3.4208	0.2536	0.7866	0.0313	0.0165
11246	0.6629	0.0083	0.4423	4.5651	0.2626	0.8979	0.0316	0.0105
N	29	30	30	30	30	30	30	30
MEAN	0.6831	0.0088	0.3767	3.6890	0.2165	0.8266	0.0314	0.0535
S.D.	0.0688	0.0019	0.0775	0.6555	0.0329	0.1432	0.0036	0.0176
S.F.	0.0128	0.0004	0.0141	0.1197	0.0060	0.0261	0.0007	0.0032

# KEY FOR INCIDENCE TABLES

+ = Present  
1 = Minimal  
2 = Mild  
3 = Moderate  
4 = Marked  
o = Tissue Missing  
N/A = Nonapplicable  
- = Negative

TABLE II-D-45

## 90-DAY TOXICITY STUDY IN RATS

## DCPD

## INCIDENCE OF HISTOLOGIC FINDINGS

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
	11005	11013	11018	11019	11020	11035	11038	11047	11048	11053	11200	11201	11205	11207	11212	11226	11234	11240	11241	11243
Tissue Findings																				
<u>Thyroid</u>	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Lung</u>																				
Chronic murine pneumonia	3	3	3	3	1	3	-	-	1	-	2	1	1	3	-	3	1	2	1	2
<u>Heart</u>																				
Focal chronic myocarditis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	2	-	-	-	-
Vacuolar myocardial change						1														
<u>Mesenteric Lymph Node</u>	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-
<u>Liver</u>	0					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Portal mononuclear infiltration		1	1																	
Microgranuloma																				
<u>Spleen</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Pancreas</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Stomach</u>																				
Focal gastritis	1				1	-					1	1								
Focal chronic gastritis																				
Squamous hyperplasia					1															
<u>Small Intestine</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Large Intestine</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nematodiasis						+												+		
<u>Kidneys</u>	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic nephritis																				

TABLE II-D-45 (Continued)

## 90-DAY TOXICITY STUDY IN RATS

DCPD

## INCIDENCE OF HISTOLOGIC FINDINGS (Continued)

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
Animal No.	11005	11013	11018	11019	11020	11035	11038	11047	11048	11053	11200	11201	11205	11207	11212	11226	11234	11240	11241	11243
Tissue Findings																				
Adrenals	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary Bladder	-	0	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-
Testes with Epididymis	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Ovaries	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Uterus	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Hydrometra																				
Prostate	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	0	-	-	-	N/A	N/A	N/A	N/A	N/A
Chronic prostatitis																				
Seminal Vesicles	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	0	-	-	-	N/A	N/A	N/A	N/A	N/A
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brain	-	-	-	-	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	0	-	-
Thoracic Spinal Cord	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rib Junction	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eye	-	0	-	-	0	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-
Nerve with Muscle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

PART II - SECTION E  
90-DAY TOXICITY STUDY IN MICE

DCPD

LBI PROJECT NO. 2564

SUMMARY

No evidence of toxicity resulted from dietary administration of DCPD to mice at levels of 28, 91, and 273 ppm for 90 days.

1. OBJECTIVE

The purpose of this study was to characterize the subchronic toxicity of DCPD when incorporated in the diet of mice.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in mice of the ICR Swiss Albino strain obtained from Flow Laboratories, Rockville, Maryland, with body weights averaging 16.9 grams for males and 15.8 grams for females at initiation.

B. Animal Groups

The mice were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	32	32	Zero - Control
2	32	32	Low - 28 ppm
3	32	32	Medium - 91 ppm
4	32	32	High - 273 ppm

They were housed in solid-bottom cages in groups of five.

3. EXPERIMENTAL DESIGN (Continued)

C. Diet Preparation

The mice were fed Purina Rodent Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

D. Observations

Body weights and food consumption were recorded weekly for each cage group. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects. Entries were made in records only when abnormalities were noted.

E. Terminations

All survivors were killed after 13 weeks. The planned 2 and 4 week recovery period was eliminated by agreement with the Project Officer since no effects had been seen.

F. Postmortem Examinations

Each animal was subjected to a gross necropsy and any observed abnormalities were recorded. The organs listed below were weighed:

heart	kidneys	adrenals (after fixation)
liver	gonads	thyroid (after fixation)
spleen		

Suitable samples of the following organs were preserved in 10% neutral formalin:

brain	stomach	ovaries
pituitary	pancreas	uterus
thyroid	small intestine	bone marrow
lung	large intestine	urinary bladder
heart	mesenteric lymph	thoracic spinal cord
liver	node	eye
spleen	nerve with muscle	rib junction
kidneys	testes with	any unusual lesions
adrenals	epididymis	
	seminal vesicles	

### 3. EXPERIMENTAL DESIGN (Continued)

#### G. Histopathologic Examination

The tissues listed below were examined microscopically from five male and five female mice in the control and the high level test groups. Those tissues showing abnormalities at the high dosage were also examined from animals of the lower dosage groups.

brain	kidneys	mesenteric lymph node
pituitary	adrenals	testes or ovaries
thyroid	stomach	uterus or prostate
heart	pancreas	bone marrow
liver	small intestine	urinary bladder
spleen	large intestine	any unusual lesions

### 4. RESULTS

#### A. Drug Administration

No difficulty was encountered with the preparation of the diets according to plan.

#### B. Observations

All mice but one survived until planned sacrifice. The average values for body weights for each of the various groups are presented in Table II-E-46. Because of the group housing plan, weights of individual mice were not recorded. The tabulated values are averages per mouse for each cage (5). Conventional statistical analysis techniques do not apply, but it seems clear that growth was alike in all groups.

Food consumption values are presented similarly in Table II-E-47. The values again are averages per mouse for each cage (5) expressed as grams/day. No differences from controls were seen. No signs of toxicity were noted.

#### C. Recovery Phase

The two- and four-week recovery phases of the study proved to be noncontributory. Since no toxic effects developed, no "recovery" could be expected.

4. RESULTS (Continued)

D. Postmortem Examination

The weights of various organs collected at terminal necropsy are presented in Table II-E-48 as recorded and in Table II-E-49 recalculated as organ to body weight ratios. Most of the indicated differences between groups in the original data disappear in the ratio tabulation.

E. Histopathologic Examination

The tissues listed in 3G above were processed in the conventional manner for preparation of sections stained with hematoxylin and eosin for examination by a staff pathologist. The pathologist's own summary is attached. No important abnormalities were noted.

5. CONCLUSIONS

No evidence of toxicity resulted from dietary administration of DCPD to mice at levels of 28, 91, and 273 ppm for 90 days.

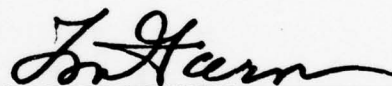
90-DAY TOXICITY STUDY IN MICE

DCPD

LBI PROJECT NO. 2564

PATHOLOGY SUMMARY

The microscopic lesions observed in this study were those routinely encountered in rats and mice. They appeared in all dosed groups and did not differ significantly from those seen in the controls.



F. M. Garner, D.V.M.

Veterinary Pathologist

Veterinary Sciences Division

TABLE 11-E-46

BODY WEIGHTS  
(grams)

GROUP MEANS

DCPD

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT																	
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
MALES																		
1 - Control																		
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32
MEAN	17.3	24.4	26.5	29.2	28.8	31.1	32.8	33.2	34.0	33.3	32.9	35.6	34.7	36.2	36.5	32.5	37.9	38.2
2 - 28 ppm																		
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	31	32	32	32	32	32	32	32
MEAN	15.0	23.0	25.6	28.4	29.2	31.4	32.6	32.9	33.5	33.0	28.4	34.0	35.0	35.6	38.9	36.7	39.8	40.8
3 - 91 ppm																		
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32
MEAN	18.0	22.3	25.3	27.7	28.0	31.5	32.6	33.2	34.1	32.0	33.3	34.4	34.7	35.2	36.1	37.1	36.5	36.6
4 - 273 ppm																		
NO. WEIGHED	32	32	32	32	32	32	32	32	32	31	31	31	31	31	31	31	31	31
MEAN	17.4	23.4	25.9	28.3	29.6	30.7	32.2	31.5	33.4	33.4	31.3	35.4	36.9	36.0	35.1	37.7	35.1	35.7

TABLE II-E-46 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS

DCPD

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT																		
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
FEMALES																			
1 - Control																			
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	10	-	5
MEAN	15.7	22.1	22.1	22.3	23.9	23.9	26.6	26.1	27.3	24.2	24.0	28.1	28.1	27.9	30.2	28.6	-	-	30.7
2 - 28 ppm																			
NO. WEIGHED	32	32	32	32	32	32	31	31	31	32	31	31	31	31	31	10	5	5	5
MEAN	15.9	21.3	20.0	23.7	24.2	23.4	25.9	25.9	26.1	24.4	19.3	27.7	27.7	28.6	28.5	27.8	30.2	30.2	30.7
3 - 91 ppm																			
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	10	-	5
MEAN	16.3	20.9	22.5	24.4	24.3	23.8	26.4	25.7	27.2	26.8	26.3	27.7	29.5	26.7	28.5	29.2	-	-	31.2
4 - 273 ppm																			
NO. WEIGHED	32	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	5	5	5
MEAN	15.2	20.3	22.2	23.3	24.1	24.3	26.8	26.5	27.3	27.2	23.1	28.5	29.5	28.4	27.8	28.4	28.8	28.8	28.8

TABLE II-E-47

FOOD CONSUMPTION  
(grams per day)

GROUP MEANS

DCPD

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	17
<u>MALES</u>																
<u>1 - Control</u>																
NO. DETN'D.	27	32	32	32	32	32	32	32	32	32	32	32	32	32	10	5
MEAN	6.2	6.4	6.1	6.1	6.1	6.2	6.2	6.1	6.0	7.4	5.7	6.5	6.0	5.3	5.7	5.4
<u>2 - 28 ppm</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	32	31	32	32	32	10	10	5
MEAN	5.4	5.6	5.9	5.7	6.3	6.3	6.2	6.2	6.5	7.5	6.2	6.3	5.9	5.8	5.9	5.6
<u>3 - 91 ppm</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	32	32	32	32	32	10	10	5
MEAN	3.7	5.3	5.3	5.9	6.0	6.1	6.0	6.0	6.3	6.2	6.3	6.3	6.3	5.4	5.4	4.8
<u>4 - 273 ppm</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	31	31	31	31	31	10	10	5
MEAN	5.0	4.9	5.4	5.5	6.3	6.2	5.6	5.7	5.9	6.5	5.9	5.7	5.4	5.4	5.6	4.9

TABLE II-E-47 (Continued)

FOOD CONSUMPTION  
(grams per day)

GROUP MEANS

DCPD

GROUP NO. & DOSAGE LEVEL	WEEKS OF TREATMENT															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	17
<u>FEMALES</u>																
<u>1 - Control</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	5
MEAN	6.1	5.5	5.8	5.5	6.0	5.8	6.1	5.7	5.3	7.1	6.0	6.3	5.9	5.5	6.0	5.9
<u>2 - 28 ppm</u>																
NO. DETN'D.	32	32	32	32	32	31	31	31	32	31	31	31	31	10	10	5
MEAN	4.9	5.7	6.1	6.8	7.3	7.6	5.6	8.4	6.7	9.1	7.6	6.7	9.0	5.8	5.7	5.9
<u>3 - 91 ppm</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	5
MEAN	5.5	6.0	6.2	6.5	6.7	6.5	6.8	6.3	6.5	6.8	6.1	6.2	6.6	6.1	6.1	6.2
<u>4 - 273 ppm</u>																
NO. DETN'D.	32	32	32	32	32	32	32	32	32	32	32	32	32	32	10	5
MEAN	4.9	6.3	6.3	6.2	6.6	6.3	6.3	6.1	6.3	7.7	6.8	6.6	6.7	4.8	5.5	5.0

TABLE II-E-48

ORGAN WEIGHTS IN MALE MICE  
(grams)

## GROUP 1 - CONTROL

## DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
817	30.6	0.0020	0.2160	1.5820	0.0790	0.5230	0.0040	0.4230
818	36.8	0.0030	0.2660	2.2300	0.1150	0.5890	0.0	0.3520
819	32.1	0.0030	0.2150	2.1200	0.0810	0.5700	0.0070	0.4380
820	28.3	0.0030	0.2090	1.9650	0.1250	0.5800	0.0	0.4420
821	34.6	0.0030	0.2900	2.1330	0.0680	0.6900	0.0060	0.3890
822	39.1	0.0050	0.2390	2.6150	0.1380	0.8350	0.0080	0.4090
823	39.6	0.0040	0.2370	3.0130	0.1390	0.7490	0.0060	0.4050
824	39.3	0.0040	0.1970	2.4750	0.1250	0.7210	0.0060	0.3770
825	38.2	0.0050	0.1890	2.8970	0.1400	0.7870	0.0090	0.4010
826	37.0	0.0060	0.2400	2.7720	0.1320	0.7820	0.0	0.4290
827	29.6	0.0	0.4050	2.2210	0.3510	0.7800	0.0	0.0
828	27.6	0.0	0.1620	2.1960	0.0720	0.6720	0.0070	0.0
829	39.0	0.0	0.2010	3.2000	0.3590	0.9900	0.0	0.0
830	33.2	0.0	0.1760	2.1940	0.0980	0.5830	0.0	0.3830
831	40.8	0.0	0.2400	2.8030	0.1160	0.9450	0.0110	0.5280
832	38.6	0.0	0.2280	2.4250	0.1250	0.7160	0.0110	0.9910
833	29.5	0.0020	0.2010	2.2140	0.0900	0.7170	0.0	0.3900
834	37.4	0.0	0.1910	2.7210	0.1930	0.7710	0.0080	0.3770
835	35.1	0.0	0.1840	2.3520	0.1280	0.6430	0.0050	0.4270
836	31.5	0.0	0.1830	2.2010	0.0980	0.5690	0.0040	1.0210
837	38.2	0.0	0.2190	2.1860	0.1670	0.6930	0.0050	1.2770
838	37.9	0.0	0.1910	2.4830	0.1270	0.6780	0.0060	0.5050
839	41.4	0.0	0.2700	3.2190	0.2040	0.8220	0.0	1.0280
840	33.9	0.0	0.2260	2.5260	0.0950	0.7250	0.0080	0.3440
841	36.5	0.0	0.1870	2.8060	0.1140	0.8020	0.0	0.3440
842	39.1	0.0040	0.3010	2.1830	0.1430	0.6800	0.0	0.4960
843	33.4	0.0030	0.2910	2.4160	0.1710	0.5900	0.0050	0.3210
844	42.2	0.0050	0.3000	3.5060	0.2020	0.9180	0.0110	0.5020
845	38.5	0.0080	0.6240	2.9900	0.5160	1.0720	0.0	0.7310
846	36.2	0.0100	0.2220	2.9090	0.1480	0.7720	0.0090	0.3660
847	39.4	0.0090	0.3140	2.6900	0.2150	0.7840	0.0070	0.4430
848	36.3	0.0070	0.3250	2.6190	0.1180	0.7440	0.0110	0.3380
N	32	18	32	32	32	32	21	29
MEAN	36.0	0.0048	0.2481	2.5269	0.1560	0.7341	0.0073	0.5130
S.D.	4.0	0.0024	0.0869	0.4153	0.0937	0.1274	0.0023	0.2474
S.E.	0.7	0.0006	0.0154	0.0734	0.0166	0.0225	0.0005	0.0459

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 2 - 28 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
881	40.1	0.0060	0.2110	2.2730	0.1180	0.9180	0.0	0.4380
882	43.1	0.0030	0.2960	3.1090	0.1400	0.9610	0.0	0.3850
883	37.5	0.0050	0.2690	2.8180	0.1340	0.6650	0.0040	0.3560
884	37.9	0.0050	0.2540	2.3150	0.1260	0.7600	0.0060	0.3960
885	36.1	0.0040	0.2590	2.7120	0.1850	0.7310	0.0	0.4110
886	38.8	0.0040	0.2510	2.2150	0.0960	0.7300	0.0100	0.4060
887	37.0	0.0040	0.3100	2.7000	0.1350	0.7110	0.0090	0.3430
888	42.9	0.0040	0.3860	3.0780	0.1240	0.9140	0.0090	0.4180
889	44.1	0.0050	0.4190	2.9960	0.1570	0.7870	0.0	0.4290
890	45.7	0.0040	0.3100	3.0730	0.1130	0.7270	0.0120	0.4070
891	33.4	0.0	0.1650	2.0080	0.0780	0.6410	0.0	0.4060
892	33.0	0.0	0.1780	2.2710	0.0810	0.7260	0.0080	0.2860
893	39.1	0.0	0.2170	2.6520	0.0970	0.7620	0.0070	0.3570
894	42.3	0.0030	0.2270	3.6520	0.1520	0.8810	0.0060	0.3750
895	37.1	0.0	0.1840	2.2580	0.0810	0.6270	0.0	0.5390
896	36.5	0.0040	0.2190	2.7250	0.0920	0.6660	0.0090	0.4370
897	39.4	0.0030	0.2600	2.5170	0.1010	0.6720	0.0	0.4940
898	32.8	0.0020	0.2250	2.0490	0.1140	0.4910	0.0060	0.3730
899	34.0	0.0020	0.2680	2.3660	0.1330	0.7970	0.0	0.4370
900	29.4	0.0040	0.2540	1.8750	0.1650	0.5460	0.0	0.4590
901	31.8	0.0	0.2140	1.6600	0.1040	0.6340	0.0	0.4300
902	40.8	0.0	0.3100	2.5850	0.1290	0.7260	0.0	0.5050
903	37.1	0.0050	0.2930	2.6500	0.1380	0.7700	0.0	0.4580
904	36.7	0.0060	0.3220	2.6070	0.1780	0.7350	0.0	0.4620
905	35.4	0.0	0.2390	2.1970	0.1290	0.6370	0.0	0.5260
906	36.0	0.0030	0.3140	2.6910	0.1040	0.7100	0.0	0.4450
907	43.0	0.0	0.4140	3.1490	0.1440	0.8440	0.0	0.5870
908	38.2	0.0040	0.2990	3.1120	0.1460	0.7760	0.0080	0.4730
909	37.8	0.0	0.2720	2.5720	0.1100	0.6010	0.0	0.4280
910	34.8	0.0040	0.2770	2.5090	0.1220	0.5970	0.0060	0.4290
911	38.2	0.0040	0.2440	2.1530	0.0900	0.7600	0.0090	0.4470
912	35.6	0.0050	0.2990	2.2600	0.0920	0.6400	0.0	0.4540
N	32	23	32	32	32	32	14	32
MEAN	37.7	0.0040	0.2706	2.5562	0.1221	0.7232	0.0078	0.4311
S.D.	3.8	0.0011	0.0607	0.4303	0.0279	0.1068	0.0021	0.0601
S.E.	0.7	0.0002	0.0107	0.0761	0.0049	0.0189	0.0006	0.0106

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 3 - 91 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
945	38.2	0.0060	0.2340	2.4420	0.0940	0.6950	0.0	0.3610
946	35.9	0.0060	0.2840	2.2760	0.1100	0.6540	0.0	0.3760
947	38.2	0.0040	0.2940	2.7050	0.1180	0.7690	0.0070	0.3860
948	39.4	0.0	0.3750	2.8420	0.1340	1.0970	0.0120	0.3390
949	33.9	0.0080	0.3050	2.4230	0.0950	0.7030	0.0090	0.3680
950	36.4	0.0040	0.3190	2.3420	0.1590	0.6590	0.0	0.4340
951	31.5	0.0080	0.2890	2.1880	0.1910	0.6280	0.0	0.4430
952	40.3	0.0060	0.2880	2.8860	0.1520	0.7370	0.0110	0.4350
953	33.0	0.0060	0.3040	2.8580	0.1570	0.7240	0.0060	0.4130
954	42.3	0.0040	0.3100	2.2220	0.1250	0.6540	0.0080	0.4060
955	33.8	0.0	0.3140	1.7430	0.0780	0.6090	0.0070	0.4360
956	32.2	0.0040	0.3060	2.1340	0.1280	0.6000	0.0100	0.3800
957	35.9	0.0040	0.3130	2.6410	0.1220	0.7540	0.0070	0.4590
958	37.4	0.0050	0.2460	2.3400	0.1140	0.7010	0.0060	0.5200
959	30.6	0.0040	0.2310	1.9950	0.1200	0.5650	0.0	0.3980
960	35.0	0.0040	0.1850	1.9790	0.0450	0.6160	0.0060	0.4450
961	35.6	0.0050	0.2460	2.4720	0.0750	0.5870	0.0	0.4550
962	34.0	0.0	0.2070	2.3930	0.1340	0.6350	0.0050	0.4150
963	32.0	0.0	0.2190	2.0560	0.1090	0.5370	0.0	0.3810
964	37.3	0.0060	0.2360	2.4760	0.1060	0.6070	0.0070	0.4490
965	44.0	0.0040	0.3500	2.4120	0.0980	0.5530	0.0060	0.3810
966	39.2	0.0060	0.2980	3.2170	0.1450	0.6600	0.0	0.5000
967	27.7	0.0030	0.2510	1.1930	0.1060	0.3900	0.0	0.4680
968	35.3	0.0060	0.2610	2.3360	0.1250	0.6580	0.0060	0.3350
969	73.4	0.0060	0.2090	2.0540	0.1230	0.5780	0.0080	0.4910
970	36.3	0.0050	0.3290	2.4610	0.1130	0.7070	0.0	0.3930
971	35.4	0.0	0.3110	2.5350	0.0730	0.6960	0.0070	0.4670
972	34.6	0.0	0.2570	2.4660	0.1160	0.5450	0.0	0.4550
973	39.8	0.0060	0.3050	2.7330	0.1550	0.9600	0.0	0.4500
974	40.0	0.0040	0.2740	2.2550	0.1950	0.6830	0.0	0.5700
975	40.4	0.0040	0.2300	2.5200	0.1380	0.6420	0.0030	0.3160
976	37.4	0.0	0.2040	2.3330	0.1130	0.7040	0.0050	0.3650
N	32	25	32	32	32	32	19	32
MEAN	37.4	0.0051	0.2747	2.3727	0.1208	0.6671	0.0072	0.4216
S.D.	7.5	0.0013	0.0463	0.3711	0.0318	0.1218	0.0022	0.0565
S.E.	1.3	0.0003	0.0082	0.0656	0.0056	0.0215	0.0005	0.0100

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN MALE MICE  
(grams)

GROUP 4 - 273 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1009	38.3	0.0	0.1770	2.4130	0.1010	0.7530	0.0060	0.3720
1010	34.9	0.0050	0.2350	2.1880	0.0820	0.5820	0.0060	0.3510
1011	42.0	0.0060	0.1750	2.9290	0.1370	0.8480	0.0070	0.3700
1012	41.3	0.0070	0.2200	2.6090	0.1370	0.6790	0.0090	0.3760
1013	40.5	0.0040	0.2430	3.2240	0.2370	0.7510	0.0070	0.4190
1014	34.5	0.0030	0.2560	2.0140	0.1250	0.5690	0.0040	0.3620
1015	37.5	0.0060	0.2530	2.4790	0.1490	0.7790	0.0050	0.4180
1016	38.2	0.0070	0.3190	2.5330	0.1240	0.8190	0.0070	0.4340
1017	32.5	0.0070	0.2790	2.1650	0.1120	0.5860	0.0080	0.3330
1018	37.9	0.0020	0.2920	2.5990	0.1580	0.8020	0.0050	0.3970
1019	36.5	0.0040	0.1980	2.2240	0.1300	0.6930	0.0080	0.4390
1020	32.8	0.0200	0.1620	1.9830	0.0970	0.6440	0.0200	0.2760
1021	34.5	0.0	0.2390	1.8370	0.1190	0.6000	0.0060	0.4470
1022	33.9	0.0040	0.2390	2.1790	0.1270	0.6860	0.0030	0.4150
1023	37.3	0.0060	0.2090	2.2520	0.1170	0.8100	0.0050	0.4920
1024	34.4	0.0	0.2190	2.0160	0.1850	0.5850	0.0	0.4850
1025	40.0	0.0030	0.2500	2.5400	0.1680	0.7290	0.0	0.5290
1026	25.7	0.0040	0.1500	1.4610	0.0460	0.3490	0.0100	0.3210
1027	37.8	0.0040	0.3070	2.2520	0.1470	0.6530	0.0070	0.4500
1028	37.7	0.0	0.2310	2.6350	0.1010	0.6220	0.0	0.5880
1030	37.9	0.0050	0.1750	2.7420	0.1430	0.7560	0.0050	0.3660
1031	35.8	0.0050	0.2100	2.3980	0.1440	0.6570	0.0140	0.4170
1032	37.4	0.0030	0.2660	2.3290	0.1190	0.7770	0.0070	0.4620
1033	36.9	0.0040	0.2310	2.7430	0.1490	0.7120	0.0080	0.3990
1034	39.7	0.0050	0.2360	2.3160	0.1120	0.8020	0.0	0.4920
1035	35.0	0.0	0.2840	2.2040	0.0	0.5620	0.0080	0.3930
1037	44.6	0.0110	0.3080	2.7620	0.3210	0.8710	0.0060	0.4950
1038	35.8	0.0070	0.3360	3.0020	0.1290	0.7680	0.0130	0.4670
1039	34.0	0.0	0.2700	2.3800	0.1170	0.6630	0.0060	0.4400
1040	34.5	0.0	0.2690	2.4000	0.1170	0.6600	0.0060	0.4100
N	30	23	30	30	29	30	26	30
MEAN	36.7	0.0057	0.2413	2.3936	0.1362	0.6922	0.0075	0.4205
S.D.	3.5	0.0037	0.0473	0.3625	0.0490	0.1097	0.0035	0.0655
S.E.	0.6	0.0008	0.0086	0.0662	0.0091	0.0200	0.0007	0.0120

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

## GROUP 1 - CONTROL

## DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
849	34.4	0.0050	0.2100	2.4790	0.1480	0.6330	0.0090	0.0540
850	26.2	0.0010	0.1750	1.4570	0.0690	0.3930	0.0050	0.0270
851	24.8	0.0050	0.1440	1.6310	0.0590	0.3990	0.0080	0.0140
852	25.0	0.0020	0.1610	1.6310	0.1380	0.4050	0.0050	0.0140
853	28.6	0.0050	0.2180	1.9850	0.1250	0.4560	0.0	0.0270
854	29.1	0.0030	0.1410	1.9130	0.0810	0.4180	0.0	0.0530
855	32.0	0.0040	0.1950	2.0160	0.1380	0.4920	0.0080	0.0590
857	30.1	0.0040	0.1710	1.8650	0.1370	0.4800	0.0100	0.0670
858	26.9	0.0040	0.1880	1.7700	0.1410	0.5320	0.0100	0.0520
859	26.5	0.0	0.1660	1.2990	0.1160	0.3880	0.0080	0.0320
860	25.1	0.0	0.2330	1.4260	0.0530	0.3740	0.0110	0.0190
861	26.6	0.0040	0.2440	1.5810	0.1250	0.3580	0.0	0.0360
862	25.7	0.0060	0.1970	1.5520	0.1150	0.3690	0.0100	0.0270
863	27.7	0.0	0.1990	1.5780	0.0870	0.4410	0.0090	0.0360
864	29.9	0.0	0.2130	1.9720	0.1260	0.5290	0.0090	0.0160
865	29.9	0.0030	0.1900	2.2100	0.1520	0.5040	0.0	0.0240
866	29.6	0.0050	0.2350	2.0870	0.1690	0.4710	0.0110	0.0240
867	28.6	0.0160	0.2180	1.9550	0.1350	0.4330	0.0210	0.0230
868	29.9	0.0120	0.1440	2.2300	0.1370	0.4920	0.0120	0.0130
869	28.6	0.0040	0.1550	1.6420	0.1230	0.4180	0.0130	0.0440
870	29.9	0.0120	0.1780	2.0110	0.1380	0.4120	0.0140	0.0290
871	26.8	0.0040	0.1790	1.4320	0.0470	0.3380	0.0090	0.0120
872	29.5	0.0060	0.1590	1.9040	0.1530	0.5150	0.0100	0.0110
873	35.8	0.0050	0.1750	2.6310	0.1080	0.5570	0.0100	0.0460
874	28.4	0.0040	0.1750	1.7220	0.0800	0.4770	0.0100	0.0360
875	29.1	0.0060	0.1980	1.8910	0.1250	0.4200	0.0	0.0250
876	30.1	0.0100	0.1650	1.8690	0.0880	0.3780	0.0150	0.0160
877	32.2	0.0060	0.4590	2.6040	0.3990	0.7220	0.0110	0.2470
878	33.8	0.0040	0.4790	2.5770	0.4010	0.8280	0.0090	0.2880
879	26.2	0.0	0.1340	1.5790	0.1210	0.4360	0.0100	0.0240
880	29.6	0.0050	0.1420	1.9030	0.1350	0.4290	0.0140	0.0260
N	31	26	31	31	31	31	26	31
MEAN	28.9	0.0056	0.2013	1.8839	0.1345	0.4676	0.0104	0.0458
S.D.	2.7	0.0033	0.0773	0.3554	0.0774	0.1054	0.0032	0.0612
S.E.	0.5	0.0007	0.0139	0.0638	0.0139	0.0189	0.0006	0.0110

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 2 - 28 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
913	29.5	0.0	0.1520	1.8940	0.1310	0.5040	0.0090	0.0180
914	23.7	0.0	0.1190	1.0740	0.0660	0.3120	0.0100	0.0130
915	39.2	0.0040	0.1560	1.7930	0.1260	0.5050	0.0120	0.0200
916	24.7	0.0030	0.1360	1.9000	0.0580	0.3670	0.0090	0.0350
917	28.5	0.0050	0.1580	1.7900	0.1260	0.3830	0.0100	0.0280
918	29.4	0.0030	0.2700	1.9950	0.1870	0.5070	0.0	0.0400
919	28.7	0.0050	0.2220	1.9950	0.1840	0.3920	0.0130	0.0340
920	29.4	0.0	0.1960	1.9950	0.1420	0.4380	0.0100	0.0320
921	27.9	0.0050	0.2160	2.1010	0.1010	0.4810	0.0120	0.0520
922	30.8	0.0060	0.2290	1.7850	0.0890	0.5120	0.0	0.0340
923	28.6	0.0	0.1310	1.5150	0.1190	0.4310	0.0120	0.0120
924	26.2	0.0060	0.1710	1.7800	0.1130	0.5010	0.0	0.1450
925	20.9	0.0040	0.1160	1.5090	0.1090	0.3360	0.0	0.0170
926	35.3	0.0	0.2130	2.2520	0.1750	0.5720	0.0	0.0190
927	27.8	0.0050	0.1320	1.7950	0.1010	0.4530	0.0080	0.0280
928	27.7	0.0060	0.1440	1.5290	0.1060	0.4320	0.0100	0.0160
929	26.6	0.0	0.1820	1.6150	0.0720	0.4030	0.0120	0.0260
930	26.9	0.0080	0.1610	2.1750	0.1000	0.4250	0.0140	0.0200
931	28.1	0.0060	0.1730	1.9380	0.0970	0.5000	0.0120	0.0260
932	29.1	0.0060	0.2110	1.8520	0.1310	0.4760	0.0120	0.0250
933	24.9	0.0050	0.1900	1.3690	0.0830	0.3930	0.0100	0.0290
934	30.1	0.0050	0.1780	1.7380	0.1480	0.4600	0.0	0.0200
935	27.9	0.0070	0.1920	1.7320	0.1410	0.4350	0.0	0.0280
936	28.9	0.0050	0.2380	1.7920	0.1350	0.4840	0.0100	0.0600
937	27.3	0.0030	0.2190	1.6140	0.0990	0.4180	0.0120	0.0310
938	36.4	0.0060	0.1840	2.1080	0.1070	0.4490	0.0120	0.0230
939	38.8	0.0050	0.2380	2.9700	0.1780	0.6230	0.0	0.0230
940	29.1	0.0080	0.4630	2.2240	0.3800	0.7490	0.0110	0.0320
941	28.0	0.0060	0.4770	2.0100	0.3830	0.6460	0.0	0.2120
942	31.5	0.0080	0.5200	2.2600	0.3450	0.7390	0.0130	0.2190
943	32.3	0.0	0.1920	2.2300	0.1580	0.5780	0.0120	0.0400
N	31	24	31	31	31	31	22	31
MEAN	28.9	0.0054	0.2122	1.8816	0.1448	0.4808	0.0111	0.0438
S.D.	3.5	0.0014	0.0990	0.3415	0.0818	0.1031	0.0015	0.0515
S.E.	0.6	0.0003	0.0178	0.0613	0.0147	0.0185	0.0003	0.0092

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 3 - 91 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
977	27.3	0.0040	0.2200	1.8300	0.1300	0.5200	0.0120	0.0350
978	28.9	0.0040	0.2340	1.8100	0.1000	0.4890	0.0090	0.0420
979	28.6	0.0040	0.1770	1.7920	0.2000	0.4720	0.0110	0.0230
980	30.6	0.0030	0.2300	1.9050	0.1590	0.5280	0.0110	0.0650
981	26.5	0.0030	0.2190	1.4920	0.1270	0.4300	0.0100	0.0640
982	29.3	0.0	0.1410	1.6820	0.1330	0.4310	0.0090	0.0180
983	29.6	0.0040	0.1800	1.7600	0.1100	0.4100	0.0120	0.0200
984	34.5	0.0	0.1960	2.2980	0.1660	0.5470	0.0120	0.0180
985	28.2	0.0060	0.1640	1.6810	0.1580	0.4250	0.0110	0.0230
986	30.6	0.0050	0.1660	1.8160	0.1250	0.5230	0.0110	0.0230
987	28.3	0.0050	0.2170	1.5930	0.1170	0.4590	0.0	0.0300
988	30.4	0.0	0.2240	2.1010	0.1490	0.5180	0.0080	0.0240
989	26.3	0.0030	0.1760	1.6040	0.1160	0.4130	0.0080	0.0090
990	31.4	0.0030	0.2160	1.9510	0.1940	0.4810	0.0110	0.0170
991	28.6	0.0040	0.2240	1.7390	0.1290	0.4930	0.0110	0.0400
992	33.2	0.0020	0.1610	2.2220	0.1480	0.5050	0.0090	0.0400
993	29.8	0.0030	0.2420	2.2040	0.1600	0.4330	0.0080	0.0520
994	30.6	0.0040	0.1970	2.3070	0.1400	0.4570	0.0	0.0390
995	28.9	0.0020	0.1670	1.8910	0.1010	0.4470	0.0	0.0330
996	25.0	0.0040	0.1740	1.5620	0.0700	0.3510	0.0080	0.0300
997	23.4	0.0020	0.1230	1.1340	0.0510	0.3340	0.0050	0.0310
998	26.8	0.0030	0.1980	1.6510	0.1030	0.3990	0.0130	0.0170
999	26.0	0.0	0.1600	1.4510	0.0940	0.3340	0.0080	0.0230
1000	28.2	0.0040	0.1800	1.8830	0.1300	0.3680	0.0100	0.0160
1001	30.5	0.0030	0.1830	1.8650	0.1260	0.4100	0.0090	0.0240
1002	30.0	0.0	0.1760	1.6800	0.1550	0.5000	0.0090	0.0740
1003	29.8	0.0040	0.1500	1.8700	0.0700	0.4800	0.0110	0.0200
1004	24.7	0.0040	0.1500	1.6100	0.1000	0.4200	0.0100	0.0120
1005	28.7	0.0	0.1870	1.7400	0.0740	0.4480	0.0100	0.0400
1006	27.8	0.0050	0.2300	1.5300	0.0860	0.4500	0.0080	0.0200
1007	30.2	0.0020	0.2200	1.5700	0.1450	0.5130	0.0	0.0780
1008	27.9	0.0040	0.2190	1.7380	0.1050	0.4890	0.0090	0.0430
N	32	26	32	32	32	32	28	32
MEAN	28.8	0.0036	0.1907	1.7801	0.1241	0.4524	0.0098	0.0326
S.D.	2.3	0.0010	0.0310	0.2553	0.0350	0.0569	0.0017	0.0178
S.E.	0.4	0.0002	0.0055	0.0451	0.0062	0.0101	0.0003	0.0031

TABLE II-E-48 (Continued)

ORGAN WEIGHTS IN FEMALE MICE  
(grams)

GROUP 4 - 273 ppm

DCPD

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1041	32.0	0.0050	0.1470	1.6060	0.1230	0.4840	0.0110	0.0390
1042	29.8	0.0050	0.1450	1.6490	0.1880	0.4370	0.0120	0.0260
1043	30.7	0.0070	0.1460	2.0370	0.1470	0.5060	0.0110	0.0230
1044	27.2	0.0040	0.1090	1.5510	0.1180	0.3980	0.0	0.0260
1045	25.9	0.0060	0.1310	1.6850	0.1080	0.3510	0.0100	0.0350
1046	30.1	0.0	0.1330	1.5130	0.0580	0.4290	0.0110	0.0060
1047	28.5	0.0	0.1670	1.8430	0.1200	0.5140	0.0090	0.0120
1048	29.3	0.0030	0.1360	1.8940	0.0860	0.4150	0.0	0.0080
1049	29.2	0.0070	0.1620	1.9100	0.1460	0.5230	0.0	0.0350
1050	30.7	0.0040	0.2440	2.1390	0.1910	0.4990	0.0130	0.0400
1051	27.7	0.0050	0.1920	2.0230	0.1060	0.4670	0.0090	0.0350
1052	31.6	0.0060	0.2400	2.4200	0.1160	0.5900	0.0130	0.0220
1053	30.9	0.0050	0.2520	2.1460	0.0960	0.5270	0.0050	0.0310
1054	28.4	0.0050	0.1780	1.9740	0.1430	0.4190	0.0130	0.0190
1055	27.1	0.0050	0.1970	1.7710	0.1070	0.3720	0.0110	0.0010
1056	28.1	0.0060	0.1510	1.2410	0.1530	0.4090	0.0080	0.0270
1057	25.9	0.0160	0.1620	1.4440	0.0790	0.4130	0.0120	0.0430
1058	29.0	0.0060	0.1460	1.6810	0.0790	0.4230	0.0100	0.0210
1059	32.9	0.0030	0.1860	1.7940	0.0790	0.5470	0.0110	0.0210
1060	30.6	0.0030	0.1640	1.9490	0.1160	0.5390	0.0090	0.0190
1061	32.7	0.0030	0.2140	1.7290	0.1200	0.4900	0.0090	0.0240
1062	31.6	0.0030	0.2080	1.8170	0.1150	0.4830	0.0280	0.0120
1063	30.4	0.0020	0.1900	1.8450	0.1020	0.4940	0.0080	0.0140
1064	33.2	0.0050	0.1930	2.1880	0.1390	0.5410	0.0	0.0210
1065	32.5	0.0070	0.1560	2.0290	0.1760	0.4960	0.0070	0.0190
1066	28.2	0.0030	0.4320	1.9320	0.3370	0.6590	0.0120	0.2440
1067	28.0	0.0040	0.2080	1.9670	0.1070	0.4300	0.0170	0.0280
1068	29.0	0.0040	0.2310	2.0200	0.1140	0.4590	0.0100	0.0520
1069	27.3	0.0050	0.2190	1.8980	0.1370	0.4380	0.0080	0.0320
1070	26.0	0.0030	0.2060	1.8070	0.0900	0.4010	0.0110	0.0170
1071	31.7	0.0050	0.2040	2.1730	0.3680	0.5630	0.0110	0.2600
1072	27.2	0.0030	0.1780	1.9870	0.1000	0.5750	0.0	0.0400
N	32	30	32	32	32	32	27	32
MEAN	29.5	0.0049	0.1886	1.8644	0.1333	0.4778	0.0111	0.0391
S.D.	2.1	0.0025	0.0573	0.2428	0.0654	0.0695	0.0041	0.0570
S.E.	0.4	0.0005	0.0101	0.0429	0.0116	0.0123	0.0008	0.0101

TABLE II-E-49

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

## GROUP 1 - CONTROL

## DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
R17	0.0065	0.7059	5.1699	0.2582	1.7091	0.0131	1.3824
R18	0.0082	0.7228	6.0598	0.3125	1.6005	0.0	0.9565
R19	0.0093	0.6698	6.6044	0.2523	1.7757	0.0218	1.3645
R20	0.0106	0.7385	6.9435	0.4417	2.0495	0.0	1.5618
R21	0.0087	0.8382	6.1647	0.1965	1.9942	0.0173	1.1243
R22	0.0128	0.6113	6.6880	0.3529	2.1355	0.0205	1.0460
R23	0.0101	0.5985	7.6086	0.3510	1.8914	0.0152	1.0227
R24	0.0102	0.5013	6.2977	0.3181	1.8346	0.0153	0.9593
R25	0.0131	0.4948	7.5838	0.3665	2.0602	0.0236	1.0497
R26	0.0162	0.6486	7.4919	0.3568	2.1135	0.0	1.1595
R27	0.0	1.3682	7.5034	1.1858	2.6351	0.0	0.0
R28	0.0	0.5870	7.9565	0.2609	2.4348	0.0254	0.0
R29	0.0	0.5154	8.2051	0.9205	2.5385	0.0	0.0
R30	0.0	0.5301	6.6084	0.2952	1.7560	0.0	1.1536
R31	0.0	0.5882	6.8701	0.2843	2.3162	0.0270	1.2941
R32	0.0	0.5907	6.2824	0.3238	1.8549	0.0285	2.5674
R33	0.0068	0.6814	7.5051	0.3051	2.4305	0.0	1.3220
R34	0.0	0.5107	7.2754	0.5160	2.0615	0.0214	1.0080
R35	0.0	0.5242	6.7008	0.3647	1.8319	0.0142	1.2165
R36	0.0	0.5810	6.9873	0.3111	1.8063	0.0127	3.2413
R37	0.0	0.5733	5.7225	0.4372	1.8141	0.0131	3.3429
R38	0.0	0.5040	6.5514	0.3351	1.7889	0.0158	1.3325
R39	0.0	0.6522	7.7754	0.4928	1.9855	0.0	2.4831
R40	0.0	0.6667	7.4513	0.2802	2.1386	0.0236	1.0147
R41	0.0	0.5123	7.6877	0.3123	2.1973	0.0	0.9425
R42	0.0102	0.7698	5.5831	0.3657	1.7391	0.0	1.2685
R43	0.0090	0.8713	7.2335	0.5120	1.7665	0.0150	0.9611
R44	0.0118	0.7109	8.3081	0.4787	2.1754	0.0261	1.1896
R45	0.0209	1.6208	7.7662	1.3403	2.7844	0.0	1.8987
R46	0.0276	0.6133	8.0359	0.4088	2.1326	0.0249	1.0110
R47	0.0228	0.7970	6.8274	0.5457	1.9898	0.0178	1.1244
R48	0.0193	0.8953	7.2149	0.3251	2.0496	0.0303	0.9311
N	18	32	32	32	32	21	29
MEAN	0.0130	0.6935	7.0208	0.4315	2.0435	0.0201	1.4114
S.D.	0.0060	0.2397	0.7822	0.2548	0.2871	0.0056	0.6606
S.E.	0.0014	0.0424	0.1383	0.0450	0.0507	0.0012	0.1227

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 2 - 28 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
881	0.0150	0.5262	5.6683	0.2943	2.2893	0.0	1.0923
882	0.0070	0.6868	7.1926	0.3248	2.2297	0.0	0.8933
883	0.0133	0.7173	7.5147	0.3573	1.7733	0.0107	0.9493
884	0.0132	0.6702	6.1082	0.3325	2.0053	0.0158	1.0449
885	0.0111	0.7175	7.5125	0.5125	2.0249	0.0	1.1385
886	0.0103	0.6469	5.7088	0.2474	1.8814	0.0258	1.0464
887	0.0108	0.8378	7.2973	0.3649	1.9216	0.0243	0.9270
888	0.0093	0.8998	7.1748	0.2890	2.1305	0.0210	0.9744
889	0.0113	0.9501	6.7936	0.3560	1.7846	0.0	0.9728
890	0.0088	0.6783	6.7243	0.2473	1.5908	0.0263	0.8906
891	0.0	0.4940	6.0120	0.2335	1.9192	0.0	1.2156
892	0.0	0.5394	6.8818	0.2455	2.2000	0.0242	0.8667
893	0.0	0.5550	6.7826	0.2481	1.9488	0.0179	0.9130
894	0.0071	0.5366	8.6336	0.3593	2.0827	0.0142	0.8865
895	0.0	0.4960	6.0863	0.2183	1.6900	0.0	1.4528
896	0.0110	0.6000	7.4657	0.2521	1.8247	0.0247	1.1973
897	0.0076	0.6599	6.3883	0.2563	1.7056	0.0	1.2538
898	0.0061	0.6860	6.2469	0.3476	1.4970	0.0183	1.1372
899	0.0059	0.7882	6.9588	0.3912	2.3441	0.0	1.2853
900	0.0136	0.8639	6.3775	0.5612	1.8571	0.0	1.5612
901	0.0	0.6730	5.2201	0.3270	1.9937	0.0	1.3522
902	0.0	0.7598	6.3358	0.3162	1.7794	0.0	1.2377
903	0.0135	0.7898	7.1429	0.3720	2.0755	0.0	1.2345
904	0.0163	0.8774	7.1035	0.4850	2.0027	0.0	1.2589
905	0.0	0.6751	6.2062	0.3644	1.7994	0.0	1.4859
906	0.0083	0.8722	7.4750	0.2889	1.9722	0.0	1.2361
907	0.0	0.9628	7.3233	0.3349	1.9628	0.0	1.3651
908	0.0105	0.7827	8.1466	0.3822	2.0314	0.0209	1.2382
909	0.0	0.7196	6.8042	0.2910	1.5899	0.0	1.1323
910	0.0115	0.7960	7.2098	0.3506	1.7155	0.0172	1.2328
911	0.0105	0.6387	5.6361	0.2356	1.9895	0.0236	1.1702
912	0.0140	0.8399	6.3483	0.2584	1.7978	0.0	1.2753
N	23	32	32	32	32	14	32
MEAN	0.0107	0.7168	6.7650	0.3264	1.9191	0.0203	1.1537
S.D.	0.0029	0.1313	0.7544	0.0814	0.2031	0.0048	0.1865
S.F.	0.0006	0.0232	0.1334	0.0144	0.0359	0.0013	0.0330

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 3 - 91 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
945	0.0157	0.6126	6.3927	0.2461	1.8194	0.0	0.9450
946	0.0167	0.7911	6.3398	0.3064	1.8217	0.0	1.0474
947	0.0105	0.7696	7.0812	0.3089	2.0131	0.0183	1.0105
948	0.0	0.9518	7.2132	0.3401	2.7843	0.0305	0.8604
949	0.0236	0.8997	7.1475	0.2802	2.0737	0.0265	1.0855
950	0.0110	0.8764	6.4341	0.4368	1.8104	0.0	1.1923
951	0.0254	0.9175	6.9460	0.6063	1.9937	0.0	1.4063
952	0.0149	0.7146	7.1613	0.3772	1.8288	0.0273	1.0794
953	0.0182	0.9364	8.6606	0.4758	2.1939	0.0182	1.2515
954	0.0095	0.7329	5.2530	0.2955	1.5461	0.0199	0.9598
955	0.0	0.9290	5.1568	0.2308	1.8018	0.0207	1.2899
956	0.0124	0.9503	6.6273	0.3975	1.8634	0.0311	1.1901
957	0.0111	0.8719	7.3565	0.3398	2.1003	0.0195	1.2786
958	0.0134	0.6578	6.2567	0.3048	1.8743	0.0160	1.3904
959	0.0131	0.7549	6.5196	0.3922	1.8464	0.0	1.3007
960	0.0114	0.5286	5.6543	0.1286	1.7600	0.0171	1.2714
961	0.0140	0.6910	6.9438	0.2107	1.6489	0.0	1.2781
962	0.0	0.6088	7.0382	0.3941	1.8676	0.0147	1.2206
963	0.0	0.6844	6.4250	0.3406	1.6781	0.0	1.1906
964	0.0161	0.6327	6.6381	0.2842	1.6273	0.0188	1.2038
965	0.0091	0.7955	5.4818	0.2227	1.2568	0.0136	0.8659
966	0.0153	0.7602	8.2066	0.3699	1.6837	0.0	1.2755
967	0.0108	0.9061	4.3069	0.3827	1.4079	0.0	1.6895
968	0.0170	0.7394	6.6176	0.3541	1.8640	0.0170	0.9490
969	0.0082	0.2847	2.7984	0.1676	0.7875	0.0109	0.6689
970	0.0138	0.9063	6.7796	0.3113	1.9477	0.0	1.0826
971	0.0	0.8785	7.1610	0.2062	1.9661	0.0198	1.3192
972	0.0	0.7428	7.1272	0.3353	1.6908	0.0	1.3150
973	0.0151	0.7663	6.8668	0.3894	2.4121	0.0	1.1307
974	0.0100	0.6850	5.6375	0.4875	1.7075	0.0	1.4250
975	0.0099	0.5693	6.2376	0.3416	1.5891	0.0074	0.7822
976	0.0	0.5455	6.2380	0.3021	1.8824	0.0134	0.9759
N	25	32	32	32	32	19	32
MEAN	0.0138	0.7529	6.4545	0.3302	1.8171	0.0189	1.1538
S.D.	0.0042	0.1517	1.0829	0.0969	0.3361	0.0062	0.2124
S.E.	0.0008	0.0268	0.1914	0.0171	0.0594	0.0014	0.0375

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN MALE MICE

GROUP 4 - 273 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
1009	0.0	0.4621	6.3003	0.2637	1.9661	0.0157	0.9713
1010	0.0143	0.6734	6.2693	0.2350	1.6676	0.0172	1.0057
1011	0.0143	0.4167	6.9738	0.3262	2.0190	0.0167	0.8810
1012	0.0169	0.5327	6.3172	0.3317	1.6441	0.0218	0.9104
1013	0.0099	0.6000	7.9605	0.5852	1.8543	0.0173	1.0346
1014	0.0087	0.7420	5.8377	0.3623	1.6493	0.0116	1.0493
1015	0.0160	0.6747	6.6107	0.3973	2.0773	0.0133	1.1147
1016	0.0183	0.8351	6.6309	0.3246	2.1440	0.0183	1.1361
1017	0.0215	0.8585	6.6615	0.3446	1.8031	0.0246	1.0246
1018	0.0053	0.7704	6.8575	0.4169	2.1161	0.0132	1.0475
1019	0.0110	0.5425	6.0932	0.3562	1.8986	0.0219	1.2027
1020	0.0610	0.4939	6.0457	0.2957	1.9634	0.0610	0.8415
1021	0.0	0.6928	5.3246	0.3449	1.7391	0.0174	1.2957
1022	0.0118	0.7050	6.4277	0.3746	2.0236	0.0088	1.2242
1023	0.0161	0.5603	6.0375	0.3137	2.1716	0.0134	1.3190
1024	0.0	0.6366	5.8605	0.5378	1.7006	0.0	1.4099
1025	0.0075	0.6250	6.3500	0.4200	1.8225	0.0	1.3225
1026	0.0156	0.5837	5.6848	0.1790	1.3580	0.0389	1.2490
1027	0.0106	0.8122	5.9577	0.3889	1.7275	0.0185	1.1905
1028	0.0	0.6127	6.9894	0.2679	1.6499	0.0	1.5597
1030	0.0132	0.4617	7.2348	0.3773	1.9947	0.0132	0.9657
1031	0.0140	0.5866	6.6983	0.4022	1.8352	0.0391	1.1648
1032	0.0080	0.7112	6.2273	0.3182	2.0775	0.0187	1.2353
1033	0.0108	0.6260	7.4336	0.4038	1.9295	0.0217	1.0813
1034	0.0125	0.5945	5.8338	0.2821	2.0202	0.0	1.2393
1035	0.0	0.8114	6.2971	0.0	1.6057	0.0229	1.1229
1037	0.0247	0.6406	6.1928	0.7197	1.9529	0.0135	1.1099
1038	0.0196	0.9385	8.3855	0.3603	2.1453	0.0363	1.3045
1039	0.0	0.7941	7.0000	0.3441	1.9500	0.0176	1.2941
1040	0.0	0.7797	6.9565	0.3391	1.9130	0.0174	1.1884
N	23	30	30	29	30	26	30
MEAN	0.0157	0.6608	6.5150	0.3660	1.8807	0.0212	1.1499
S.D.	0.0109	0.1289	0.6649	0.1050	0.1949	0.0112	0.1625
S.E.	0.0023	0.0235	0.1214	0.0195	0.0356	0.0022	0.0297

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

## GROUP 1 - CONTROL

## DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
849	0.0145	0.6105	7.2064	0.4302	1.8401	0.0262	0.1570
850	0.0038	0.6679	5.5611	0.2634	1.5000	0.0191	0.1031
851	0.0202	0.5806	6.5766	0.2379	1.6089	0.0323	0.0565
852	0.0080	0.6440	6.5240	0.5520	1.6200	0.0200	0.0560
853	0.0175	0.7622	6.9406	0.4371	1.5944	0.0	0.0944
854	0.0103	0.4845	6.5739	0.2784	1.4364	0.0	0.1821
855	0.0125	0.6094	6.3000	0.4313	1.5375	0.0250	0.1844
857	0.0133	0.5681	6.1960	0.4551	1.5947	0.0332	0.2226
858	0.0149	0.6989	6.5799	0.5242	1.9777	0.0372	0.1933
859	0.0	0.6264	4.9019	0.4377	1.4642	0.0302	0.1208
860	0.0	0.9283	5.6813	0.2112	1.4900	0.0438	0.0757
861	0.0150	0.9173	5.9436	0.4699	1.3459	0.0	0.1353
862	0.0233	0.7665	6.0389	0.4475	1.4358	0.0389	0.1051
863	0.0	0.7184	5.6968	0.3141	1.5921	0.0325	0.1300
864	0.0	0.7124	6.5953	0.4214	1.7692	0.0301	0.0535
865	0.0100	0.6355	7.3913	0.5084	1.6856	0.0	0.0803
866	0.0169	0.7939	7.0507	0.5709	1.5912	0.0372	0.0811
867	0.0559	0.7622	6.8357	0.4720	1.5140	0.0734	0.0804
868	0.0401	0.4816	7.4582	0.4582	1.6455	0.0401	0.0435
869	0.0140	0.5420	5.7413	0.4301	1.4615	0.0455	0.1538
870	0.0401	0.5953	6.7258	0.4615	1.3779	0.0468	0.0970
871	0.0149	0.6679	5.3433	0.1754	1.2612	0.0336	0.0448
872	0.0203	0.5390	6.4542	0.5186	1.7458	0.0339	0.0373
873	0.0140	0.4888	7.3492	0.3017	1.5559	0.0279	0.1285
874	0.0141	0.6162	6.0634	0.2817	1.6796	0.0352	0.1268
875	0.0206	0.6804	6.4983	0.4296	1.4433	0.0	0.0859
876	0.0332	0.5482	6.2093	0.2924	1.2558	0.0498	0.0532
877	0.0186	1.4255	8.0870	1.2391	2.2422	0.0342	0.7671
878	0.0118	1.4172	7.6243	1.1864	2.4497	0.0266	0.8521
879	0.0	0.5115	6.0267	0.4618	1.6641	0.0382	0.0916
880	0.0169	0.4797	6.4290	0.4561	1.4493	0.0473	0.0878
N	26	31	31	31	31	26	31
MEAN	0.0190	0.6929	6.4711	0.4566	1.6074	0.0361	0.1510
S.D.	0.0114	0.2264	0.7119	0.2267	0.2533	0.0110	0.1824
S.E.	0.0022	0.0407	0.1279	0.0407	0.0455	0.0022	0.0328

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 2 - 28 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
913	0.0	0.5153	6.4203	0.4441	1.7085	0.0305	0.0610
914	0.0	0.5021	4.5316	0.2785	1.3165	0.0422	0.0549
915	0.0132	0.5166	5.9371	0.4172	1.6722	0.0397	0.0662
916	0.0121	0.5506	7.6923	0.2348	1.4858	0.0364	0.1417
917	0.0175	0.5544	6.2807	0.4421	1.3439	0.0351	0.0982
918	0.0102	0.9184	6.7857	0.6361	1.7245	0.0	0.1361
919	0.0174	0.7735	6.9512	0.6411	1.3659	0.0453	0.1185
920	0.0	0.6667	6.7857	0.4830	1.4898	0.0340	0.1088
921	0.0179	0.7742	7.5305	0.3620	1.7240	0.0430	0.1864
922	0.0195	0.7435	5.7955	0.2890	1.6623	0.0	0.1104
923	0.0	0.4580	5.2972	0.4161	1.5070	0.0420	0.0420
924	0.0229	0.6527	6.7939	0.4313	1.9122	0.0	0.5534
925	0.0191	0.5550	7.2201	0.5215	1.6077	0.0	0.0813
926	0.0	0.6034	6.3796	0.4958	1.6204	0.0	0.0538
927	0.0180	0.4748	6.4568	0.3633	1.6295	0.0288	0.1007
928	0.0217	0.5199	5.5199	0.3827	1.5596	0.0361	0.0578
929	0.0	0.6842	6.0714	0.2707	1.5150	0.0451	0.0977
930	0.0297	0.5985	8.0855	0.3717	1.5799	0.0520	0.0743
931	0.0214	0.6157	6.8968	0.3452	1.7794	0.0427	0.0925
932	0.0206	0.7251	6.3643	0.4502	1.6357	0.0412	0.0859
933	0.0201	0.7631	5.4980	0.3333	1.5783	0.0402	0.1165
934	0.0166	0.5914	5.7741	0.4917	1.5282	0.0	0.0664
935	0.0251	0.6882	6.2079	0.5054	1.5591	0.0	0.1004
936	0.0173	0.8235	6.2007	0.4671	1.6747	0.0346	0.2076
937	0.0110	0.8022	5.9121	0.3626	1.5311	0.0440	0.1136
938	0.0165	0.5055	5.7912	0.2940	1.2335	0.0330	0.0632
939	0.0129	0.6134	7.6546	0.4588	1.6057	0.0	0.0593
940	0.0275	1.5911	7.6426	1.3058	2.5739	0.0378	0.1100
941	0.0214	1.7036	7.1786	1.3679	2.3071	0.0	0.7571
942	0.0254	1.6508	7.1746	1.0952	2.3460	0.0413	0.6952
943	0.0	0.5944	6.9040	0.4892	1.7895	0.0372	0.1238
N	24	31	31	31	31	22	31
MEAN	0.0190	0.7332	6.5076	0.4983	1.6635	0.0392	0.1527
S.D.	0.0050	0.3253	0.8117	0.2723	0.2884	0.0055	0.1776
S.E.	0.0010	0.0584	0.1458	0.0489	0.0518	0.0012	0.0319

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 3 - 91 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
977	0.0147	0.8059	6.7033	0.4762	1.9048	0.0440	0.1282
978	0.0138	0.8097	6.2630	0.3460	1.6920	0.0311	0.1453
979	0.0140	0.6189	6.2657	0.6993	1.6503	0.0385	0.0804
980	0.0098	0.7516	6.2255	0.5196	1.7255	0.0359	0.2124
981	0.0113	0.8264	5.6302	0.4792	1.6226	0.0377	0.2415
982	0.0	0.4812	5.7406	0.4539	1.4710	0.0307	0.0614
983	0.0135	0.6081	5.9459	0.3716	1.3851	0.0405	0.0676
984	0.0	0.5681	6.6609	0.4812	1.5855	0.0348	0.0522
985	0.0213	0.5816	5.9610	0.5603	1.5071	0.0390	0.0816
986	0.0163	0.5425	5.9346	0.4085	1.7091	0.0359	0.0752
987	0.0177	0.7668	5.6290	0.4134	1.6219	0.0	0.1060
988	0.0	0.7368	6.9112	0.4901	1.7039	0.0263	0.0789
989	0.0114	0.6692	6.0989	0.4411	1.5703	0.0304	0.0342
990	0.0096	0.6879	6.2134	0.6178	1.5318	0.0350	0.0541
991	0.0140	0.7832	6.0804	0.4510	1.7238	0.0385	0.1399
992	0.0060	0.4849	6.6928	0.4458	1.5211	0.0271	0.1205
993	0.0101	0.8121	7.3960	0.5369	1.4530	0.0268	0.1745
994	0.0131	0.6438	7.5392	0.4575	1.4935	0.0	0.1275
995	0.0064	0.5779	6.5432	0.3495	1.5467	0.0	0.1142
996	0.0160	0.6960	6.2480	0.2800	1.4040	0.0320	0.1200
997	0.0085	0.5256	4.8462	0.2179	1.4274	0.0214	0.1325
998	0.0112	0.7388	6.1604	0.3843	1.4888	0.0485	0.0634
999	0.0	0.6154	5.5808	0.3615	1.2846	0.0308	0.0885
1000	0.0142	0.6383	6.6773	0.4610	1.3050	0.0355	0.0567
1001	0.0098	0.6000	6.1148	0.4131	1.3443	0.0295	0.0787
1002	0.0	0.5867	5.6000	0.5167	1.6667	0.0300	0.2467
1003	0.0134	0.5034	6.2752	0.2343	1.6107	0.0369	0.0671
1004	0.0162	0.6073	6.5182	0.4049	1.7004	0.0405	0.0486
1005	0.0	0.6516	6.0627	0.2578	1.5610	0.0348	0.1394
1006	0.0180	0.8273	5.5036	0.3094	1.6187	0.0288	0.0719
1007	0.0066	0.7285	5.1987	0.4801	1.6987	0.0	0.2583
1008	0.0143	0.7849	6.2294	0.3763	1.7527	0.0323	0.1541
N	25	32	32	32	32	28	32
MEAN	0.0128	0.6644	6.1703	0.4280	1.5713	0.0340	0.1132
S.D.	0.0037	0.1064	0.5692	0.1056	0.1430	0.0058	0.0602
S.E.	0.0007	0.0188	0.1006	0.0187	0.0253	0.0011	0.0106

TABLE II-E-49 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES IN FEMALE MICE

GROUP 4 - 273 ppm

DCPD

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
1041	0.0156	0.4594	5.0187	0.3844	1.5125	0.0344	0.1219
1042	0.0168	0.4866	5.5336	0.6309	1.4664	0.0403	0.0872
1043	0.0228	0.4756	6.6352	0.4788	1.6482	0.0358	0.0749
1044	0.0147	0.4007	5.7022	0.4338	1.4632	0.0	0.0956
1045	0.0232	0.5058	6.5058	0.4170	1.3552	0.0386	0.1351
1046	0.0	0.4419	5.0266	0.1927	1.4252	0.0365	0.0199
1047	0.0	0.5860	6.4667	0.4211	1.8035	0.0316	0.0421
1048	0.0102	0.4642	6.4642	0.2935	1.4164	0.0	0.0273
1049	0.0240	0.5548	6.5411	0.5000	1.7911	0.0	0.1199
1050	0.0130	0.7948	6.9674	0.6221	1.6254	0.0423	0.1303
1051	0.0181	0.6931	7.3032	0.3827	1.6859	0.0325	0.1264
1052	0.0190	0.7595	7.6582	0.3671	1.8671	0.0411	0.0696
1053	0.0162	0.8155	6.9450	0.3107	1.7055	0.0162	0.1003
1054	0.0176	0.6268	6.9507	0.5035	1.4754	0.0458	0.0669
1055	0.0185	0.7269	6.5351	0.3948	1.3727	0.0406	0.0037
1056	0.0214	0.5374	4.4164	0.5445	1.4555	0.0285	0.0961
1057	0.0618	0.6255	5.5753	0.3050	1.5946	0.0463	0.1660
1058	0.0207	0.5034	5.7965	0.2724	1.4586	0.0345	0.0724
1059	0.0091	0.5653	5.4529	0.2401	1.6626	0.0334	0.0638
1060	0.0098	0.5490	6.3693	0.3791	1.7614	0.0294	0.0621
1061	0.0092	0.6544	5.2875	0.3670	1.4985	0.0275	0.0734
1062	0.0095	0.6582	5.7500	0.3639	1.5285	0.0886	0.0380
1063	0.0066	0.6250	6.0491	0.3355	1.6250	0.0263	0.0461
1064	0.0151	0.5813	6.5404	0.4187	1.6295	0.0	0.0633
1065	0.0215	0.4800	6.2431	0.5415	1.5262	0.0215	0.0585
1066	0.0106	1.5319	6.8511	1.1950	2.3369	0.0426	0.8652
1067	0.0143	0.7429	7.0250	0.3821	1.5357	0.0607	0.1000
1068	0.0138	0.7966	6.9655	0.3931	1.5828	0.0345	0.1793
1069	0.0183	0.8022	6.9524	0.5018	1.6044	0.0293	0.1172
1070	0.0115	0.7923	6.9500	0.3462	1.5423	0.0423	0.0654
1071	0.0158	0.6562	6.8549	1.1609	1.7760	0.0347	0.8202
1072	0.0110	0.6544	7.3051	0.3676	2.1140	0.0	0.1471
N	30	32	32	32	32	27	32
MEAN	0.0170	0.6421	6.3346	0.4515	1.6202	0.0376	0.1330
S.D.	0.0097	0.2026	0.7743	0.2152	0.2073	0.0134	0.1908
S.E.	0.0018	0.0358	0.1369	0.0380	0.0366	0.0026	0.0337

TABLE II-E-50

KEY FOR INCIDENCE TABLES

- + = Present
- 1 = Minimal
- 2 = Mild
- 3 = Moderate
- 4 = Marked
- o = Tissue Missing
- N/A = Nonapplicable
- = Negative

TABLE II-E-50

## 90-DAY TOXICITY STUDY IN MICE

DCPD

## INCIDENCE OF HISTOLOGIC FINDINGS

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
Animal No.	832	845	846	847	848	867	868	870	873	879	1020	1030	1031	1037	1038	1053	1057	1062	1065	1067
Tissue Findings																				
Thyroid	0	0	0	0	0	0	-	-	-	0	-	-	-	-	-	-	-	0	0	-
Heart	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesenteric Lymph Node	0	-	-	-	-	-	-	-	-	-	-	-	-	2	-	0	-	2	-	-
Lymphocytic hyperplasia								+												
Lymphoreticular hyperplasia												+								
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Periportal infiltrate						1														
Microgranuloma								+												
Spleen	-	-	-	-	-	-	0	-	-	-	-	-	-	+	-	-	0	-	-	-
Malignant lymphoma																				
Pancreas	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Islet hyperplasia, focal					+															
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Small intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymphoid hyperplasia		1																		
Large intestine	+	+	+	-	+	+	-	-	-	+	+	+	+	-	-	+	-	-	-	+
Nematodiasis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kidneys																				

TABLE II-E-50 (Continued)

## 90-DAY TOXICITY STUDY IN MICE

DCPD

## INCIDENCE OF HISTOLOGIC FINDINGS (Continued)

Group No.	1 - Male					1 - Female					4 - Male					4 - Female				
	832	845	846	847	848	867	868	870	873	879	1020	1030	1031	1037	1038	1053	1057	1062	1065	1067
Tissue Findings																				
Adrenal Glands	-	-	-	-	-*	-	-*	-	-	-	-	-	-*	-	-	0	-	-	-	-
Urinary Bladder	-	0	-	-	-	0	0	0	-	-	-	-	-	-	-	0	-	-	-	0
Testes with Epididymis	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Ovaries	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Uterus	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-
Acute purulent cervicitis																	2			
Metritis																				
Prostate	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A	-	-	-	-	-	N/A	N/A	N/A	N/A	N/A
Focal hyperplasia																				
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-
Others																				
Eye**																				
Corneal amyloid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

\* One only

\*\* Microscopic examination made only when gross abnormality found.

PART II - SECTION F  
14-DAY TOXICITY STUDY IN DOGS

DCPD

LBI PROJECT NO. 2565

SUMMARY

Feeding of DCPD to male and female dogs for 14 days at 40, 125, and 375 ppm in the diet did not lead to development of evidence of toxicity.

1. OBJECTIVE

The purpose of this study was to characterize the subchronic toxicity of DCPC in dogs.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in beagle dogs obtained from Hazleton Research Animals, Cumberland, Virginia, with body weights averaging 9.2 kg for males and 8.1 kg for females at initiation.

B. Animal Groups

The dogs were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dietary Levels</u>
	<u>Male</u>	<u>Female</u>	
1	1	1	Zero - Control
2	1	1	Low - 40 ppm
3	1	1	Medium - 125 ppm
4	1	1	High - 375 ppm

C. Diet Preparation

The dogs were fed Purina Dog Chow in meal form into which the test compound was blended at the designated levels. Fresh diets were prepared weekly.

D. Observations

Body weights and food consumption were recorded weekly. Daily observations for mortality were made and weekly records were maintained of appearance, behavior, and signs of toxic or pharmacologic effects.

3. EXPERIMENTAL DESIGN (continued)

E. Clinical Laboratory Measurements

The following determinations were made on all dogs initially and again just before termination:

Hematology

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	

Clinical Biochemistry

blood sugar	SGPT
blood urea nitrogen (BUN)	SGOT
total protein	alkaline phosphatase
total bilirubin	

Urinalysis

pH	ketones
specific gravity	total protein
glucose	

F. Termination and Postmortem Examination

Upon conclusion of the study, the animals were killed and subjected to careful gross necropsy under the supervision of a veterinary pathologist. The following organs were removed and weighed individually:

thyroid	spleen	testes with epididymis
heart	kidneys	ovaries
liver	adrenals	

Samples of the following tissues were taken for preservation in 10% neutral formalin:

mammary gland	stomach	uterus
thyroid	small intestine	bone marrow
lung	large intestine	brain
heart	kidneys	pituitary
liver	adrenals	thoracic spinal cord
gall	urinary bladder	eye
spleen	testes	nerve with muscle
pancreas	ovary	rib junction
mesenteric lymph node	prostate	any unusual lesions

3. EXPERIMENTAL DESIGN (continued)

F. Termination and Postmortem Examination

The following tissues from each animal in the control and the high dosage groups were prepared and examined for histopathologic alteration:

thyroid	spleen	adrenals
lung	stomach	bone marrow
heart	small intestine	brain
liver	kidney	lesions

4. RESULTS

All dogs survived the period of the study without incidence of adverse effect.

All clinical laboratory determinations resulted in values within the limits of normal.

Body weights fluctuated somewhat as is felt to be normal for adult dogs. Food consumption also varied in a normal way.

Terminal sacrifice and all aspects of the postmortem examination were conducted under the supervision of Herman R. Seibold, V.M.D., of Bionetics' Pathology Department. These tabulations of organ weights and gross and microscopic postmortem findings and a signed summary are attached. He reports no noteworthy deviations.

5. CONCLUSIONS

Feeding of DCPD to male and female dogs for 14 days at 40, 125, and 375 ppm in the diet did not lead to development of evidence of toxicity.

14-DAY TOXICITY STUDY IN DOGS

DCPD

LBI PROJECT NO. 2565

Summary of the Gross and Histological Examination of Tissue

Tissues from the control and high dose experimental animals were examined microscopically. Tissues, animal identification, drug identification and dose are listed in tables on (1) Necropsy Observations and (2) Histological findings.

Repeated abnormality was found only in mesenteric lymph nodes and was recognized in the gross, as reddening of the medullary area (on section of the node) and microscopically, as hemorrhage and erythrophagocytosis. The incidence of the hemorrhage and erythrophagocytosis, among principals versus controls did not indicate a relation with the treatments. The mesenteric nodes had not been specified (in the protocol) for microscopic examination, consequently only the nodes with gross abnormalities were examined microscopically.

In no instance did an organ or tissue specified for microscopic examination present a noteworthy difference in microscopic appearance from corresponding organs or tissues of the dogs in the same group or in different groups.

Date

March 25, 1976

H. R. Seibold  
Herman R. Seibold, V.M.D.  
Pathologist

TABLE II-F-51

BODY WEIGHTS  
(Kilograms)

DCPD

<u>DOG NO.</u>	<u>SEX</u>	<u>INTERVAL</u>		
		<u>WK 0</u>	<u>WK 1</u>	<u>WK 2</u>
<u>GROUP 1 - CONTROL</u>				
260	M	8.2	9.2	8.6
255	F	8.4	8.7	8.9
<u>GROUP 2 - 40 ppm</u>				
261	M	8.8	9.8	9.6
254	F	8.2	8.8	8.4
<u>GROUP 3 - 125 ppm</u>				
266	M	9.8	10.3	9.9
256	F	7.6	8.2	8.2
<u>GROUP 4 - 375 ppm</u>				
262	M	10.0	10.8	10.6
258	F	-	8.2	7.6

TABLE II-F-52  
FOOD CONSUMPTION  
(Kilograms)

DCPD

<u>DOG NO.</u>	<u>SEX</u>	<u>INTERVAL</u>		
		<u>WK 1</u>	<u>WK 2</u>	<u>WK 3</u>
<u>GROUP 1 - CONTROL</u>				
260	M	2.7	2.8	1.6
255	F	1.7	1.7	1.3
<u>GROUP 2 - 40 ppm</u>				
261	M	2.6	2.3	1.8
254	F	1.3	1.4	1.0
<u>GROUP 3 - 125 ppm</u>				
266	M	2.5	2.0	1.2
256	F	1.5	1.8	1.6
<u>GROUP 4 - 375 ppm</u>				
262	M	1.7	1.6	1.7
258	F	1.7	1.2	1.0

TABLE II-F-53

## HEMATOCYTOLOGY

PRE-DRUG - DCPD

DOG NO.	SEX	CELL VOL. %	HEMO-GLOBIN gm %	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	My	Juv	Ban	DIFFERENTIAL (%)*						
									Seg	LY	Mo	Eo	Bas	AtL	
GROUP 1 - CONTROL															
260	M	50.0	17.3	7.26	10.9	0	0	0	64	29	1	6	0	3	
255	F	46.0	15.9	8.00	15.3	0	0	0	46	52	0	2	0	2	
GROUP 2 - 40 ppm															
261	M	46.0	15.8	6.60	10.7	0	0	0	56	36	1	7	0	2	
254	F	51.0	17.8	7.97	18.9	0	0	0	60	38	1	1	0	0	
GROUP 3 - 125 ppm															
266	M	50.0	16.9	7.10	15.1	0	0	0	49	41	1	9	0	5	
256	F	50.5	17.0	7.77	14.9	0	0	1	44	45	3	7	0	0	
GROUP 4 - 375 ppm															
262	M	47.0	16.3	6.87	8.4	0	0	0	54	35	4	7	0	2	
258	F	52.0	17.5	8.55	10.3	0	0	0	53	46	1	0	0	0	

\* Differential (%) - My = Myelocytes; Juv = Juveniles; Ban = Bands; Seg = Segmented Neutrophils; Ly = Lymphocytes; Mo = Monocytes; Eo = Eosinophils; Bas = Basophils; AtL = Atypical Lymphocytes.

TABLE II-F-3) (Continued)

HEMATOCYTOLOGY														
TERMINAL - DCPD														
DOG NO.	SEX	CELL VOL. %	HEMO-GLOBIN gm %	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	My	Juv	Ban	Seg	LY	Mo	Eo	Bas	AtL
GROUP 1 - CONTROL														
260	M	51.0	17.0	7.15	9.8	0	0	0	62	34	2	2	0	0
255	F	45.0	15.1	6.91	8.5	0	0	1	40	58	0	1	0	0
GROUP 2 - 40 ppm														
261	M	48.5	16.4	6.74	12.5	0	0	0	61	38	0	1	0	0
254	F	49.0	16.8	6.99	10.5	0	0	0	49	49	2	0	0	0
GROUP 3 - 125 ppm														
266	M	51.5	17.8	7.35	14.6	0	0	0	53	41	1	5	0	0
256	F	49.5	16.4	6.74	8.2	J	0	1	55	42	1	1	0	1
GROUP 4 - 375 ppm														
262	M	45.5	15.5	7.27	8.5	0	0	0	48	39	1	12	0	0
258	F	48.0	16.1	6.59	9.5	0	0	0	63	37	0	0	0	0

\* Differential (%) - My = Myelocytes; Juv = Juveniles; Ban = Bands; Seg = Segmented Neutrophils; Ly = Lymphocytes; Mo = Monocytes; Eo = Eosinophils; Bas = Basophils; AtL = Atypical Lymphocytes.

TABLE II-F-54

## BLOOD CHEMISTRY

PRE-DRUG - DCPD

DOG NO.	SEX	BUN mg %	GLU- COSE mg %	ALK. PHOS. I.U.	SGOT I.U.	T. BILI- RUBIN mg %	TOTAL PROTEIN gm %	SGPT I.U.
<u>GROUP 1 - CONTROL</u>								
260	M	12	113	92	34	0.4	6.3	38
255	F	15	109	80	32	0.4	5.0	37
<u>GROUP 2 - 40 ppm</u>								
261	M	14	104	86	33	0.3	6.3	27
254	F	16	84	113	26	0.3	6.1	29
<u>GROUP 3 - 125 ppm</u>								
266	M	10	86	105	29	0.3	5.9	54
256	F	13	103	105	41	0.4	6.5	24
<u>GROUP 4 - 375 ppm</u>								
262	M	15	108	62	35	0.3	5.9	29
258	F	13	118	106	29	0.4	5.8	27

TABLE II-F-54 (Continued)

BLOOD CHEMISTRY															
TERMINAL - DCPD															
DOG NO.	SEX	BUN mg %	GLU- COSE mg %	ALK. PHOS. I.U.	SGOT I.U.	LDH I.U.	T.BILI- RUBIN mg %	Ca mg %	PHOS- PHORUS mg %	CREAT- ININE mg %	URIC ACID mg %	CHOLE- TEROL mg %	TOTAL PROTEIN gm %	AL- BUMIN gm %	SGPT I.U.
GROUP 1 - CONTROL															
260	M	12	101	90	42	274	0.2	10.8	5.2	0.9	0.5	135	6.3	3.9	32
255	F	15	109	77	48	182	0.2	10.6	4.9	1.0	0.5	179	5.7	3.5	47
GROUP 2 - 40 ppm															
261	M	14	88	90	39	230	0.2	10.8	6.5	0.8	0.5	131	6.0	3.4	28
254	F	15	84	99	35	126	0.2	10.5	4.7	0.9	0.5	120	5.6	3.4	42
GROUP 3 - 125 ppm															
266	M	13	81	125	60	210	0.2	10.6	6.9	0.8	0.5	170	6.0	3.7	67
256	F	14	103	110	45	185	0.2	10.1	5.1	0.9	0.5	135	6.1	3.4	32
GROUP 4 - 375 ppm															
262	M	15	109	72	37	120	0.2	10.7	5.0	0.9	0.4	130	5.5	3.3	34
258	F	12	102	88	35	75	0.1	9.9	4.4	0.9	0.4	91	5.3	3.5	29

TABLE II-F-55

URINALYSIS

KEY

Color:     Y = Yellow  
            Or = Orange  
            Br = Brown  
            Str = Straw

Casts:     fgr = Finely Granular

Crystals:  T.P. = Triple Phosphate  
            U.A. = Uric Acid  
            Ca O = Calcium Oxalate

- or 0 = None or Negative  
+ = Trace, Occasional, Rare,  
    Very Little  
1+ = Slight, Small, Little,  
    Few, Some, Light  
2+ = Moderate, Frequent, Large  
3+ = Severe, Heavy, Many  
4+ = Maximal  
TNTC = Too Numerous to Count

TABLE II-F-55

## URINALYSIS

PRE-DRUG - DCPD

DOG NO.	SEX	COLOR	APPEARANCE	SPEC. GRAV.	PH	AL-BUMIN	GLU-COSE	KE-TONES	BILI-RUBIN	OCCULT BLOOD	MICROSCOPIC EXAMINATION/HPE*										
											RBC	EPITH	CASTS	AMORPH	BACT	CRYSTALS		OTHER			
																U.A.	T.P.				
												GROUP 1 - CONTROL									
260**	M	Y	Clear	1.025	6	0	0	0	0	0	2-3	4-5	1-2	-	-	1+	-	-			
255	F	Y	Cloudy	1.030	7	0	0	0	0	0	6-7	2-3	2-3	-	-	2+	-	-			
												GROUP 2 - 40 ppm									
261	M	Y	Cloudy	1.024	7	0	0	0	0	0	0-1	-	-	-	-	-	-	-			
254	F	Y	Cloudy	1.022	8	0	0	0	0	0	3-4	0-1	-	-	-	±	-	-			
												GROUP 3 - 125 ppm									
266	M	Y	Cloudy	1.030	6	0	0	0	0	0	6-7	-	1-2	-	-	3+	-	-			
256	F	Y	Cloudy	1.035	6	0	0	0	0	0	5-6	2-3	4-5	-	-	2+	-	-			
												Group 4 - 375 ppm									
262	M	Y	Cloudy	1.028	6	0	0	0	0	0	2-3	-	1-2	-	-	-	-	-			
258	F	Y	Cloudy	1.034	6	0	0	0	0	0	6-8	1-2	0-1	0-1fgr	-	1+	-	-			

\*Microscopic examination per high power field.

\*\*Repeat value 7 days later.

TABLE II-F-55 (Continued)

## URINALYSIS

TERMINAL - DCPD

DOG NO.	SEX	COLOR	APPEARANCE	SPEC. GRAV.	pH	AL-BUMIN	GLUCOSE	KETONES	BILI-RUBIN	OCULT BLOOD	MICROSCOPIC EXAMINATION/HPF*									
											CRYSTALS									
											U.A.	T.P.	OTHER	AMORPH	BACT	CASTS	EPITH	RBC	MBC	GROUP 1 - CONTROL
260	M	Y	Cloudy	1.032	6	0	0	0	0	0	2-3	-	1-2	-	-	-	-	-	-	
255	F	Y	Cloudy	1.041	7	1+	0	0	0	0	3-4	2-3	0-1	-	-	1+	-	-	-	
GROUP 2 - 40 ppm																				
261	M	Y	Cloudy	1.025	7	±	0	0	0	0	1-2	1-2	0-1	-	-	2+	-	-	-	
254	F	Y	Cloudy	1.028	5	0	0	0	0	0	8-10	0-1	1-2	-	-	3+	-	-	-	
GROUP 3 - 125 ppm																				
266	M	Y	Cloudy	1.019	7	0	0	0	0	0	5-6	-	0-1	-	-	4+	-	-	-	
256	F	Y	Cloudy	1.033	6	0	0	0	0	0	6-8c1	4-5	3-4	-	-	2+	-	1+	-	
GROUP 4 - 375 ppm																				
262	M	Y	Cloudy	1.018	6	0	0	0	0	0	3-4	2-3	2-3	-	-	4+	-	-	-	
258	F	Y	Cloudy	1.033	6	0	0	0	0	0	8-10	3-4	2-3	-	-	1+	-	1+	-	

\*Microscopic examination per high power field.

TABLE II-F-56  
14-DAY TOXICITY STUDY IN DOGS  
HISTOLOGICAL FINDINGS  
DCPD

GROUP	1-CONTROL		4-375 PPM	
SEX	M	F	M	F
DOG NUMBER	260	255	262	258
<u>PATHOLOGY NUMBER (76-1_)</u>	470	471	476	477
<u>Tissue/Findings</u>				
Thyroid	-	-	-	-
Lung	-	-	-	-
Heart	-	-	-	-
Liver	-	-	-	-
Spleen	-	-	-	-
Mesenteric Lymph Nodes				
Hemorrhage	3		3	3
Erythrophagocytosis	3		3	-
Stomach	-	-	-	-
Small Intestine	-	-	-	-
Large Intestine	-	-	-	-
Kidneys	-	-	-	-
Adrenals	-	-	-	-
Bone Marrow	-	-	-	-
Brain	-	-	-	-

LEGEND FOR TABLE

- = tissue within normal histological limits  
3 = moderate

TABLE II-F-57  
14-DAY TOXICITY STUDY IN DOGS  
NECROPSY OBSERVATIONS  
DCPD

GROUP	1-CONTROL		2-40 PPM		3-125 PPM		4-375 PPM	
SEX	M	F	M	F	M	F	M	F
DOG NUMBER	260	255	261	254	266	256	262	258
PATHOLOGY NO. (76-1_)	470	471	472	473	474	475	476	477
<u>Tissue/Findings</u>								
Thyroid	-	-	-	-	-	-	-	-
Lung	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-
Gall bladder								
Granular mucosa	-	-	-	-	-	-	-	-
Spleen	-	-	-	-	-	-	-	-
Mesenteric Lymph Nodes								
Reddening of medullary area	3	-	3	3	3	-	3	3
Stomach	-	-	-	-	-	-	-	-
Small Intestine	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	-	-	-	-
Kidneys	-	-	-	-	-	-	-	-
Adrenals	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-

LEGEND FOR TABLE

- = gross abnormalities not observed  
3 = moderate

TABLE II-F-58  
14-DAY TOXICITY STUDY IN DOGS  
ORGAN WEIGHTS

DCPD									
<u>DOG NO.</u>	<u>SEX</u>	<u>THYROID</u>	<u>HEART</u>	<u>LIVER</u>	<u>SPLEEN</u>	<u>KIDNEYS</u>	<u>ADRENALS</u>	<u>GONADS</u>	
				<u>GROUP 1 - CONTROL</u>					
260	M	1.04	80.09	256.16	45.31	20.66(rt.) 25.17(1t.)	0.42(rt.) 0.40(1t.)	5.82(rt.) 6.79(1t.)	
255	F	0.57	61.87	233.67	45.42	20.63(rt.) 20.31(1t.)	0.48(rt.) 0.50(1t.)	0.37(rt.) 0.29(1t.)	
				<u>GROUP 2 - 40 ppm</u>					
261	M	1.09	80.77	298.05	67.68	24.82(rt.) 24.99(1t.)	0.43(rt.) 0.42(1t.)	4.85(rt.) 5.56(1t.)	
254	F	0.54	-	243.23	38.56	23.03(rt.) 22.35(1t.)	0.50(rt.) 0.45(1t.)	- 0.32(1t.)	
				<u>GROUP 3 - 125 ppm</u>					
266	M	0.86	72.80	340.52	28.37	31.32(rt.) 35.68(1t.)	0.49(rt.) 0.59(1t.)	7.01(rt.) 7.11(1t.)	
256	F	0.82	58.64	225.63	36.05	21.09(rt.) 21.80(1t.)	0.43(rt.) 0.36(1t.)	0.31(rt.) 0.25(1t.)	
				<u>GROUP 4 - 375 ppm</u>					
262	M	0.79	86.26	307.33	77.89	26.29(rt.) 25.08(1t.)	0.36(rt.) 0.39(1t.)	9.29(rt.) 9.39(1t.)	
258	F	0.63	58.77	208.90	44.88	20.62(rt.) 20.63(1t.)	0.46(rt.) 0.46(1t.)	0.26(rt.) 0.24(1t.)	

PART II - SECTION G  
PRIMARY EYE IRRITATION STUDY IN RABBITS

DCPD

LBI PROJECT NO. 2560

SUMMARY

The Draize Eye Irritation Test revealed signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Irritation was limited to the conjunctivae, but occurred in spite of irrigation at two or four seconds after the application. In all cases, the irritation was absent by Day 3.

1. OBJECTIVE

The objective of this study was to investigate the possibility that direct contamination of the eye with the test material would be followed by irritation and/or injury.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Eye irritancy was studied by direct application of the liquid material to the conjunctival sac of one eye of an albino rabbit of the New Zealand White strain. The procedure is widely known as the Draize Eye Irritation Test.

Nine rabbits were used for this study. The chosen eye (usually left) of each rabbit was stained with fluorescein and examined with the aid of magnification and fluorescent lighting to ascertain that it was clear of any lesions before application of the test material. With an assistant holding the animal and forming a pouch of the lower eyelid a sample of 0.1 ml of the material was delivered directly into the conjunctival sac. After delivery of the material, the eyelid was released and the lids gently pressed together momentarily. Following this, the treated eyes of three animals were washed with about 20 ml of lukewarm water two seconds after application; the eyes of three more animals were washed at four seconds; and the remainder were not washed. The opposite eye remained untreated and served as a control.

3. EXPERIMENTAL DESIGN (continued)

After the initial application, each eye was examined at 1, 2, 3, 4, 7 and 14 days. Observations were carried out by experienced observers and a copy of the "Illustrated Guide for Grading Eye Irritation By Hazardous Substances" was at hand during the conduct of this experiment. The scale used for scoring ocular lesions is attached.

4. RESULTS

A complete tabulation of the scores recorded for each of the nine animals used is presented in Table II-G-59. The results may be summarized by a statement that some irritation of the conjunctivae was observed in seven of the nine animals following application of the test material. Irritation was reduced but not prevented by irrigation two or four seconds after application. In all cases the irritation was confined to the conjunctivae. In all cases the eyes were normal by the third day.

5. CONCLUSIONS

The Draize Eye Irritation Test revealed signs of temporary irritation by the test compound following its application to the conjunctival sacs of albino rabbits. Irritation was limited to the conjunctivae, but occurred in spite of irrigation two or four seconds after the application. In all cases the irritation had cleared by the third day postexposure.

TABLE II-G-59  
EYE IRRITATION SCORES - RABBITS  
DCPD

		NOT IRRIGATED											
ANIMAL	OBS. TIME (DAYS)	61584				6185				6186			
		1	2	3	4	7	14	1	2	3	4	7	14
Cornea		0	0	0	0	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae		1	1	0	0	0	0	1	2	0	0	0	0
Total Score		2	2	0	0	0	0	2	4	0	0	0	0

		IRRIGATED AT 2 SECONDS											
ANIMAL	OBS. TIME (DAYS)	6188				6175				6176			
		1	2	3	4	7	14	1	2	3	4	7	14
Cornea		0	0	0	0	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae		0	0	0	0	0	0	1	1	0	0	0	0
Total Score		0	0	0	0	0	0	2	2	0	0	0	0

		IRRIGATED AT 4 SECONDS											
ANIMAL	OBS. TIME (DAYS)	6179				6181				6183			
		1	2	3	4	7	14	1	2	3	4	7	14
Cornea		0	0	0	0	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae		0	1	0	0	0	0	1	2	0	0	0	0
Total Score		0	2	0	0	0	0	2	4	0	0	0	0

# SCALE FOR SCORING OCULAR LESIONS\*

## (1) CORNEA

- (A) Opacity-degree of density (area most dense taken for reading)
- No Opacity . . . . . 0
  - Scattered or diffuse area, details of iris clearly visible . . . . 1
  - Easily discernible translucent areas, details of iris slightly obscured . . . . . 2
  - Opalescent areas, no details of iris visible, size of pupil barely discernible . . . . . 3
  - Opaque, iris invisible . . . . . 4
- (B) Area of cornea involved
- One quarter (or less) but not zero . . . . . 1
  - Greater than one quarter, but less than half . . . . . 2
  - Greater than half, but less than three quarters . . . . . 3
  - Greater than three quarters, up to whole area . . . . . 4
- Score equals A x B x 5 Total maximum = 80

## (2) IRIS

- (A) Values
- Normal . . . . . 0
  - Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reactions is positive) . . . . . 1
  - No reaction to light, hemorrhage, gross destruction (any or all of these) . . . . . 2
- Score equals A x 5 Total maximum = 10

## (3) CONJUNCTIVAE

- (A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)
- Vessels normal . . . . . 0
  - Vessels definitely injected above normal . . . . . 1
  - More diffuse, deeper crimson red, individual vessels not easily discernible . . . . . 2
  - Diffuse beefy red . . . . . 3
- (B) Chemosis
- No swelling . . . . . 0
  - Any swelling above normal (includes nictitating membrane) . . . . 1
  - Obvious swelling with partial eversion of lids . . . . . 2
  - Swelling with lids about half closed . . . . . 3
  - Swelling with lids about half closed to completely closed . . . . 4
- (C) Discharge
- No discharge . . . . . 0
  - Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) . . . . . 1
  - Discharge with moistening of the lids and hairs just adjacent to lids . . . . . 2
  - Discharge with moistening of the lids and hairs, and considerable area around the eye . . . . . 3
- Score equals (A + B + C) x 2 Total maximum = 20

The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctivae. Total maximum score possible = 110

\*Lehman, A. J., et al., Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Assoc. Food and Drug Officials of the U. S., Austin, Texas, 1959.

PART II - SECTION H  
ACUTE DERMAL IRRITATION STUDY IN RABBITS

DCPD

LBI PROJECT NO. 2561

SUMMARY

Application of DCPD to the intact and abraded skin at doses as high as 2.0 g/kg produced only minimal skin irritation and no signs of systemic intoxication.

1. OBJECTIVE

The purpose of this study was to evaluate the toxicity of DCPD following a single application to the skin of rabbits. The design of the study afforded an insight into the systemic toxicity as well as an evaluation of the potential for skin irritation.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Four male New Zealand White (albino) rabbits, obtained from B and H Rabbitry, Rockville, Maryland, were acclimated to laboratory conditions for at least two weeks. Single doses of 2.0 grams per kilogram of body weight of the undiluted test substance, DCPD, were administered by dermal application to all four male rabbits. The hair was clipped closely on the backs of all rabbits prior to application. The skin of two rabbits was abraded by making minor incisions through the stratum corneum. These incisions were not sufficient to disturb the derma and bleeding was not produced. After application of the test material to the prepared skin of the back, the area treated was covered with cotton gauze and the trunk was covered with rubber dental damming. A flange-type collar was fitted in order to limit the rabbit's access to the application.

During the acclimation period and throughout the study, the rabbits were individually housed in wire-bottom cages in temperature-controlled quarters under artificial lighting automated to provide a 12-hour light to dark cycle in each day. Purina Rabbit Chow and water were provided ad libitum.

### 3. EXPERIMENTAL DESIGN (Continued)

The rabbits were observed for mortality and other signs of intoxication on the day of application and daily thereafter for 14 days. Body weights were recorded initially and at the termination of the study. The collar and covering over the area of application were removed after 24 hours and the excess test material removed. The effect on the skin was evaluated at that time and daily thereafter until the termination of the study according to the scoring system described in the Federal Hazardous Substances Act as follows:

<u>Erythema and Eschar Formation:</u>	<u>Value</u>
No erythema.....	0
Very slight erythema (barely perceptible).....	1
Well-defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4

#### Edema Formation:

No edema.....	0
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (raised approximately 1 millimeter).....	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure).....	4

Fourteen days after treatment, the rabbits were killed with an air embolism and the organs of the thoracic and visceral cavities were examined for abnormalities.

### 4. RESULTS

No rabbits died during the 14 days following administration of the test material. There was no indication of systemic intoxication based on general appearance and behavior. The mean body weights have been tabulated below:

<u>Dose</u> g/kg	<u>Mean Body Weights (kg)</u>	
	<u>Day 0</u>	<u>Day 14</u>
2.0	2.9	3.4

These data did not indicate any compound-effect on body weight.

4. RESULTS (Continued)

There was no edema or eschar formation of the skin at any time. Three of the four rabbits showed slight erythema, which persisted seven to nine days. The skin of the back was stained yellow in two rabbits after the eighth day. Hair growth appeared normal in the shaved area on the 14th day.

At necropsy one rabbit showed some pitting and dark areas of the spleen; otherwise, no abnormalities were noted.

5. CONCLUSIONS

Following the application of a single dose of DCPD to the abraded or intact skin of rabbits at doses of 2.0 g/kg, minimal skin irritation and no systemic toxicity was observed.

PART II - SECTION I  
A TEST FOR LIVER ENZYME  
INDUCTION IN RATS

DCPD

LBI PROJECT NO. 2567

SUMMARY

The test material, DCPD, was administered orally to rats at a dietary level of 750 ppm for 4 days. The duration of hexobarbital-induced sleeping time measured on the 5th day was comparable in control and in DCPD treated rats. Body weights and liver weights were not altered by treatment with DCPD. It was concluded that DCPD was not a liver enzyme inducing agent.

1. OBJECTIVE

The purpose of this study was to test the potential of the test material to induce liver enzyme activity. The effect of pretreatment of rats with the test material on hexobarbital-induced sleep was used as a basis for this test.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Weanling Charles River COBS CD (SD) BR rats were received from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts. These test animals were housed individually in hanging wire cages and acclimated to laboratory conditions for 6 days. Water and appropriate diets were provided ad libitum.

The animals were assigned to treatment groups as indicated below:

<u>Group No.</u>	<u>Number of Rats</u>		<u>Treatment</u>
	<u>Male</u>	<u>Female</u>	
1	10	10	Control (corn oil)
2	10	10	750 ppm DCPD

The test material was incorporated into the basal diet (Purina Laboratory Chow Meal) after being dissolved in corn oil in a manner so as to provide a dietary concentration of 750 ppm. Corn oil was incorporated into the diet of the control rats in a similar manner.

3. EXPERIMENTAL DESIGN (continued)

All rats were observed frequently during the first 4 days of treatment for changes in general appearance and behavior. Body weights were obtained on Days 1 and 5 of the study.

On Day 5 of the study, 100 mg/kg of hexobarbital was administered by intraperitoneal injection to all rats and the duration of sleeping time was measured. The end point observed was based on the inability of the rat to right itself when placed on its side. After recovering from the effect of hexobarbital, all rats were killed with carbon dioxide, a gross necropsy performed, and the liver weighed.

4. RESULTS

There were no changes in general appearance of the rats during the first 4 days of treatment. Additional data (body weights, liver weights, and duration of sleeping time) have been tabulated in Table II-I-60. Analysis of these data did not suggest a difference between rats treated with DCPD and control rats.

Necropsy findings revealed pale kidneys in rats of both the treated and the control groups, but it was judged that this finding was not related to treatment with DCPD.

5. CONCLUSIONS

DCPD was judged not to be a liver enzyme inducing agent in rats.

TABLE II-I-60

## SUMMARY OF BODY WEIGHT, LIVER WEIGHT, AND SLEEPING TIME

ANIMAL NO. & SEX	BODY WEIGHT (g)		LIVER WEIGHT (g)	LIVER/BODY WEIGHT RATIO (%)	SLEEPING TIME (Minutes)
	Day 1	Day 5			
Group 1 - Control					
1849 M	80.7	110.7	6.011	5.43	44
1850 M	81.5	106.1	5.228	4.93	44
1851 M	78.0	98.8	5.735	5.80	78
1852 M	87.7	116.4	6.115	5.25	43
1853 M	79.3	107.3	6.052	5.64	47
1854 M	77.8	101.5	5.336	5.26	38
1855 M	80.7	105.0	4.748	4.52	55
1856 M	78.7	106.2	5.159	4.86	77
1857 M	83.3	107.3	4.933	4.60	61
1858 M	83.8	110.3	5.405	4.90	53
MEAN	81.15	106.96	5.472	5.12	54.00
S.E.	0.98	1.55	0.153	0.14	4.45
1859 F	63.4	82.4	4.214	5.11	46
1860 F	69.9	93.8	5.446	5.81	106
1861 F	69.1	89.5	4.773	5.33	107
1862 F	67.5	83.7	*	*	**
1863 F	64.3	86.1	4.834	5.61	64
1864 F	67.8	93.1	5.184	5.57	41
1865 F	64.8	88.3	5.134	5.81	50
1866 F	61.8	83.0	3.957	4.77	85
1867 F	69.1	91.3	4.818	5.28	28
1868 F	65.0	85.9	3.780	4.40	84
MEAN	66.27	87.71	4.682	4.85	67.89
S.E.	0.88	1.31	0.182	0.60	9.62

\*Lost Liver

\*\*Judged to have been incorrectly injected (did not sleep)

TABLE II-I-50 (Continued)

## SUMMARY OF BODY WEIGHT, LIVER WEIGHT, AND SLEEPING TIME

ANIMAL NO. & SEX	BODY WEIGHT (g)		LIVER WEIGHT (g)	LIVER/BODY WEIGHT RATIO (%)	SLEEPING TIME (Minutes)
	Day 1	Day 5			
Group 2 - DCPD					
1869 M	82.9	111.4	6.300	5.66	36
1870 M	79.9	109.5	6.075	5.53	49
1871 M	79.8	104.7	5.123	4.89	44
1872 M	82.2	109.6	5.952	5.43	*
1873 M	80.3	104.4	5.761	5.52	41
1874 M	84.6	112.0	6.114	5.46	42
1875 M	78.0	101.4	4.998	4.93	47
1876 M	77.1	106.5	6.372	5.93	48
1877 M	81.1	106.2	4.918	4.63	56
1878 M	83.8	111.0	5.671	5.11	56
MEAN	80.97	107.67	5.728	5.31	46.56
S.E.	0.77	1.12	0.171	0.13	2.22
1879 F	67.8	93.1	5.983	6.43	46
1880 F	61.7	76.7	4.589	5.98	58
1881 F	66.7	87.8	4.470	5.09	54
1882 F	68.1	90.7	4.615	5.09	34
1883 F	66.5	89.1	4.782	5.37	44
1884 F	72.5	93.7	4.543	4.85	69
1885 F	63.5	82.9	4.421	5.33	47
1886 F	63.2	80.6	3.793	4.71	60
1887 F	63.3	87.9	4.208	4.79	39
1888 F	68.2	84.1	3.738	4.44	55
MEAN	66.15	87.66	4.514	5.21	50.60
S.E.	1.03	1.76	0.196	0.19	3.33

\*Lost Liver

PART II - SECTION J  
GUINEA PIG SENSITIZATION

DCPD

LBI PROJECT NO. 2562

SUMMARY

DCPD is not a sensitizer in guinea pigs.

1. OBJECTIVE

This study was designed to evaluate the sensitizing potential of the test material.

2. MATERIAL

Refer to Part II - Section A.

3. EXPERIMENTAL DESIGN

Twelve albino guinea pigs were obtained from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts, and randomly divided into two groups: four animals to receive a known sensitizing agent, 2,4-dinitro-1-chlorobenzene, and eight animals to receive the test material DCPD. The guinea pigs were housed individually with water and food available ad libitum.

Initially, and at intervals as needed thereafter, the hair was clipped from the trunk area. A 0.1% weight/volume solution of the known sensitizing material in physiological saline was injected intracutaneously on one side of the trunk area of each control animal. The control vehicle was injected into the other side of the trunk.

A 0.1% weight/volume solution of the test material in corn oil was injected intracutaneously into one side of the trunk of each test animal. The other side was injected with the vehicle only. The control and test materials were injected three times per week until a total of ten injections had been given.

Following the last sensitizing treatment, the animals were maintained for an additional two weeks, and then a challenge dose administered. The volume of injection was 0.05 ml for the first sensitizing injection, 0.1 ml for the balance of the sensitization exposure, and 0.05 ml for the challenge dose. The site of injection was examined for irritation 24 and 48 hours after each dose and was evaluated for erythema and edema according to the Draize scoring technique as follows:

3. EXPERIMENTAL DESIGN (Continued)

Draize Scoring Technique

Erythema

0 = none

1 = well defined

2 = moderate to severe

3 = severe to slight eschar formation

Edema

0 = none

1 = slight

2 = moderate (raised ca. 1.0 mm.)

3 = severe (raised 1.0 mm.)

The average diameter of the skin response was measured with calipers at 24 and 48 hours after administration of each dose. If the intensity of the local inflammatory response or the number of animals responding was substantially greater following the challenge injection than following the sensitizing injections, the material was considered to have produced sensitization.

4. RESULTS

Reponse to initial injections of 2,4-dinitro-1-chlorobenzene ranged from zero to 5 x 5 mm in size and from no discoloration to a marked yellow-green color. Responses to the challenge injection, in all cases, were increased in area and degree of discoloration. The sizes were 2 to 15 (mathematically infinite) times the initial response in the same guinea pig. At the 48-hour observation, there was only slight reduction in response size.

Initial responses to DCPD injections were all negative. No guinea pig showed a reaction at 24 or 48 hours. Responses to challenge injections were minimal with sizes up to 8 x 8 mm but no color reaction beyond mild erythema.

5. CONCLUSIONS

DCPD is not a sensitizer in the guinea pig.

PART II - SECTION K  
MICROBIAL MUTAGENESIS  
DCPD  
LBI PROJECT NO. 2568

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NOT REPORTED AT THIS TIME--SEE FOREWORD

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PART II - SECTION L  
PHARMACOKINETICS AND METABOLISM

DCPD

LBI PROJECT NO. 2569

SUMMARY

DCPD was absorbed after oral administration to mice, rats, and dogs. Peak plasma levels occurred in 2 hours in mice and dogs, and in 6 hours in rats. DCPD was widely distributed in all three species at 1 to 2 hours with the highest levels in urinary bladder, gall bladder and body fat and in mice, in gall bladder and bile in dogs, and in body fat, adrenals and urinary bladder in rats. Excretion appeared to be primarily via the urine in all three species. About 85% of the administered radioactivity was accounted for in urine and feces within 24 hours. Urine from mice and dogs showed two radioactive components while rat urine also contained a third. All of these seemed to differ from DCPD on TLC, but none has yet been identified.

1. OBJECTIVE

The purpose of this study was to determine the rate of absorption, tissue distribution, biotransformation, and time of excretion of Dicyclopentadiene (DCPD- $^{14}\text{C}$ ) following a single oral dose given to mice, rats, and dogs.

2. MATERIAL

DPCD- $^{14}\text{C}$  (Lot No. 895-157), uniformly labeled with  $^{14}\text{C}$ , was synthesized by New England Nuclear Corporation, Boston, Massachusetts. The specific activity was 3.02  $\mu\text{Ci}/\text{mM}$  and the purity was greater than 99% as indicated by gas- and thin-layer chromatography. The total amount of 53 mg was diluted with 600 mg of nonradioactive DCPD, purchased from MC/B Manufacturing Chemists, Cincinnati, Ohio. This stock of radiolabeled compound was analyzed for radiochemical purity by thin-layer chromatography using three different solvent systems. These results showed purity >97%. This stock of DCPD- $^{14}\text{C}$  was subsequently used for all pharmacokinetic and metabolism studies.

3. EXPERIMENTAL DESIGN

A. Animals and Administration of Radiolabeled DCPD- $^{14}\text{C}$

1. Mice

Twenty-four male, Swiss Webster mice, weighing 20 to 30 grams, were fasted for 18 hours and administered a single

### 3. EXPERIMENTAL DESIGN (Continued)

#### A. Animals and Administration of Radiolabeled DCPD-<sup>14</sup>C (Continued)

##### 1. Mice (Continued)

oral dose of DCPD-<sup>14</sup>C at 40 mg/kg of body weight. This solution contained 5 mg of DCPD-<sup>14</sup>C (specific activity 1.0  $\mu$ Ci/mg) per ml of corn oil. Three mice were housed in Roth [1] glass metabolic cages with free access to food and water. Animals received a normal diet of Purina Mouse Chow. The quantitative collection of urine, feces, and expired carbon dioxide was made at various time periods. The expired carbon dioxide was absorbed by a mixture containing ethanolamine:methylcellosolve:toluene (1:8:10 v/v).

##### 2. Rats

Twelve male Sprague-Dawley rats, weighing 180 to 280 grams, were fasted for 18 hours and administered a single oral dose of DCPD-<sup>14</sup>C at 110 mg/kg of body weight. This solution contained 20 mg of DCPD-<sup>14</sup>C (specific activity 0.20  $\mu$ Ci/mg) per ml of corn oil. Rats were housed individually in Roth metabolism cages with free access to food and water. Animals received a normal diet of Purina Rat Chow. The quantitative collection of urine, feces, and expired carbon dioxide was made at various time periods. The expired carbon dioxide was absorbed by a mixture containing ethanolamine:methylcellosolve:toluene (1:8:10 v/v).

##### 3. Dogs

Five male, young adult, purebred beagle dogs (Hazleton Laboratories, Cumberland, Virginia) weighing approximately 7.6 to 8.9 kilograms were used. The dogs were kept in individual stainless steel metabolism cages and received a normal diet of Purina Dog Chow throughout the entire study. The dogs were fasted for 18 hours and were given a single oral dose of DCPD-<sup>14</sup>C at 100 mg/kg body weight. This solution contained 50 mg of DCPD-<sup>14</sup>C (specific activity 0.04  $\mu$ Ci/mg) per ml of corn oil.

#### B. Sample Collection

##### 1. Blood

Three mice were killed by an intraperitoneal injection of sodium pentobarbital at 15 minutes and at 1, 2, 4, 6, 24, 48, and 72 hours after administration of DCPD-<sup>14</sup>C. Two rats were similarly killed at 2, 4, 6, 24, 48, and 72 hours. Blood was collected from the dorsal aorta in heparinized syringes. Blood from mice was pooled for

### 3. EXPERIMENTAL DESIGN (Continued)

#### B. Sample Collection (Continued)

##### 1. Blood (Continued)

each respective time. Blood was drawn from the femoral vein of dogs at 0.5, 1, 2, 4, 6, 10, and 24 hours after administration of DCPD-<sup>14</sup>C, and at each subsequent 24-hour interval until the dog was killed. Hematocrit values were determined for all samples and plasma was separated by centrifugation at 1500 to 2000 rpm for 15 minutes. Both blood and plasma were assayed for radioactivity.

##### 2. Urine, Feces, and Expired Carbon Dioxide

Urine, feces, and expired carbon dioxide were collected from mice and rats for 24 hours as indicated above and at 24-hour intervals thereafter until all animals were killed. Urine and feces were collected from individual dogs for each 24-hour interval until the dogs were killed by intravenous injection of Lidocaine at 4, 24, 48, and 72 hours and at 7 days after administration of DCPD-<sup>14</sup>C. Total volumes or weights were recorded and all samples were subjected to radioassay according to the procedure outlined in this report.

##### 3. Tissues and Organs

The following tissues and organs were excised from individual animals at each time stated above: spleen, lungs, heart, liver, kidneys, testes, brain, abdominal muscle, fat, urinary bladder, adrenals, eyes, femur, skin, gall bladder, small intestine, large intestine, cecum, and stomach. From dogs additional samples included: medulla, cerebrum, cerebellum, thyroid, lymph nodes, spinal cord, bone marrow, pancreas, pituitary, bile, lens, cornea, ocular fluid and ocular tissue. Tissues (100 to 200 mgs) were weighed directly into combustion cones or scintillation vials and processed for radioassay.

The contents of the stomach, small intestine, cecum, and large intestine were removed with normal saline and homogenized in a Virtis tissue homogenizer. Samples (100 to 200 mgs) were used for radioassay.

The stomach, small intestine, cecum, large intestine (without contents) and carcass of the animals were suspended in 30% NaOH for two to three days with constant

### 3. EXPERIMENTAL DESIGN (Continued)

#### B. Sample Collection (Continued)

##### 3. Tissues and Organs (Continued)

stirring and then homogenized in a Virtis tissue homogenizer and Waring blender, respectively. Samples (100 to 200 mgs) were weighed directly into combustion cones or scintillation vials and processed for radioassay. All rat samples were processed individually while mice samples for each period were pooled, weighed, and treated as one sample.

#### C. Sample Preparation for Radioassay

Analysis of radioactive blood, plasma, urine, fecal homogenates, tissues, and tissue homogenates were performed by a modification of the method described by Mahin and Lofberg [2] in which xylene is substituted for toluene. Samples of blood, plasma, or urine (0.1 ml) and 100 to 200 mg of tissue, tissue homogenate, homogenate of gastrointestinal contents or fecal homogenate were placed directly into scintillation vials. All samples were run in triplicate. To the vials 0.2 ml 60% perchloric acid (analytical reagent) and 0.4 ml of 30% hydrogen peroxide were added. The samples were digested overnight in an oven at 65 to 70°C. The vials were removed and allowed to cool to room temperature. The samples were mixed with 15 ml of scintillation solution. [This solution was made by dissolving 12.0 grams of 2,5-diphenyloxazole (PPO) (Packard Instrument Company) in 2 liters of xylene (Mallinkrodt).] Radioactive measurements were made after equilibration to 3°C in a Tri-Carb liquid scintillation spectrometer, Model 3375, (Packard Instrument Company) or liquid scintillation spectrometer, LKB-8100. The  $^{14}\text{C}$  recovery was about 80% and  $^{14}\text{C}$  counting efficiency was in the range of 93 to 95%. All samples were counted with appropriate standards that were prepared by the same procedure. The counting time was selected to yield a statistical accuracy of  $1.0 \pm 2.5\%$ .

Standards were prepared by placing 0.1 or 0.2 ml aliquots of DCPD- $^{14}\text{C}$  dosing solutions into a 10 ml volumetric flask and diluting to 10 ml with methanol. Triplicate standards of 0.1 or 0.2 ml were then placed into scintillation vials. The standards were digested and counted as described previously along with the samples under investigation. Radioactivity present in the various test samples were quantitated in terms of  $\mu\text{g}$  of DCPD- $^{14}\text{C}$  per g or ml of wet tissue.

#### D. Radioassay of Expired Carbon Dioxide

Expired carbon dioxide from mice and rats was absorbed by a mixture of ethanolamine:methylcellosolve:toluene (1:8:10 v/v).

### 3. EXPERIMENTAL DESIGN (Continued)

#### D. Radioassay of Expired Carbon Dioxide (Continued)

Five ml of this mixture were placed in triplicate into scintillation vials. Ten ml of scintillation solution was added. The blank sample consisted of 5 ml of ethanolamine-methylcellosolve-toluene and 10 ml of scintillation solution. The samples were measured for radioactivity with an appropriate standard taken in 5 ml of ethanolamine-methylcellosolve-toluene. The counting time was selected to yield a statistical accuracy of  $1.0 \pm 2.5\%$ .

#### E. Extraction of Radioactivity from Urine

Ten to 20 ml of 0- to 24-hour urine samples and control urine spiked with DCPD- $^{14}\text{C}$  were extracted three times with equal volumes of diethyl ether (DEE). The DEE layer was separated from extracted urine after centrifugation for 10 minutes at 1500 to 2000 rpm. The pooled volumes of DEE and extracted urine were recorded. The original urine, the urine after extraction, and the DEE extract were analyzed for radioactivity as previously described. The resulting counts per minute were used to determine the percent radioactivity extracted by the solvent.

The DEE extracts were evaporated to dryness using a Buchler flash rotary evaporator and then residues were taken up in small volumes of methanol. These samples were further analyzed by thin-layer chromatography to determine the nature of the radioactive components.

#### F. Enzymatic Hydrolysis of Urine

Glusulase (0.1 ml) was added to 10 ml of 0- to 24-hour urine sample and control urine spiked with DCPD- $^{14}\text{C}$ . [The activity of the glusulase was tested qualitatively using glucuronide phenolphthalein as a substrate. Glusulase (0.1 ml) contained 10,242 units of sulfatase and 19,717 units of  $\beta$ -glucuronidase (Lot No. HA043B, Endo Research Laboratories, Inc., Garden City, New York).] The urine samples were incubated in a constant temperature water bath at 37C for 24 hours. After incubation, the urine samples were extracted three times with equal volumes of DEE. The original urine, extracted urine, and DEE extracts were analyzed by liquid scintillation counting to determine the percent radioactivity in the various fractions. The DEE extracts were then evaporated to dryness using a Buchler flash rotary evaporator and the residues were taken up in small volumes of methanol. The DEE extracts were subjected to thin-layer chromatography to determine the nature of the radioactive components.

#### G. Thin-Layer Chromatography of Urine

All solvents used for thin-layer chromatography (TLC) studies were analytical grade reagents. TLC plates (5 x 20 and 20 x 20 cm) were precoated with silica gel G to a thickness of 0.25

### 3. EXPERIMENTAL DESIGN (Continued)

#### G. Thin-Layer Chromatography of Urine (Continued)

mm and 0.20 mm, respectively. [Batch No. 3633643 and Batch No. 3028572, Merck and Company, Inc., Rahway, New Jersey] Total counts of 2000 to 5000 cpm in 10 to 20 ml samples were spotted. Several solvent systems were used for developing the TLC plates (see Results). The radioactive spots on the TLC plates (5 x 20 cm) were localized by scanning with a radiochromatogram scanner, Model 7201, (Packard Instrument Company) at appropriate settings for time constant (20 seconds), linear range (300 cpm), and chart speed (0.2 cm/min). Radioactivity present in each peak area was quantitated by means of a disc integrator. Radioactive spots on two dimensional TLC plates (20 x 20 cm) were localized by placing the plates on HQ-1000 X-ray film in a 8" x 10" cassette for 1 to 2 weeks. The films were developed and tracings were made of the radioactive spots that showed up on the film. In order to quantitate the radioactivity, the radioactive zones were scraped directly into scintillation vials. First the silica gel was suspended in 0.5 ml methanol and later 15 ml of scintillation fluid was added. The samples were counted and the radioactivity was calculated as percent in each zone.

### 4. RESULTS AND DISCUSSION

#### A. Blood and Plasma

The average blood and plasma levels for mice, rats, and dogs after administration of DCPD-<sup>14</sup>C are presented in II-L-61. The average plasma levels of DCPD-<sup>14</sup>C derived radioactivity were higher than blood levels at all times in all three species. The average peak plasma levels were 11.36 and 39.9 µg/ml at 2 hours in mice and dogs, and 23.28 µg/ml at 6 hours in rats. These results indicate that DCPD-<sup>14</sup>C is absorbed more rapidly in mice and dogs than in rats. The average plasma values of DCPD-<sup>14</sup>C for all three species were plotted on semilogarithmic paper as µg/ml versus time in hours. These results are presented in Figures II-L-4, II-L-5, and II-L-6. There appear to be two separate components with different half-lives and disappearance rates in all three species. The first set of components disappeared from plasma with  $T_1 \text{ } 1/2 = 4$  hours in mice, and 10 hours in dogs with respective disappearance rate constants of  $K_1 = 0.17$  and  $0.07 \text{ hours}^{-1}$ . The data obtained for rats were insufficient to make a precise evaluation of the first half-life. The second set of components had half-lives of  $T_2 \text{ } 1/2 = 18, 27, \text{ and } 18 \text{ hours}^{-1}$  with respective disappearance rate constants of  $K_2 = 0.04, 0.026 \text{ and } 0.04 \text{ hours}^{-1}$  for mice, rats and dogs, respectively. These results indicate that absorption and metabolism of DCPD-<sup>14</sup>C are similar in mice and dogs while metabolism in rats appears to be slow and complex.

TABLE II-L-61

Average Plasma and Whole Blood Levels of  $^{14}\text{C}$  Radioactivity  
in Mice, Rats, and Dogs After a Single Oral Dose of DCPD- $^{14}\text{C}$

Hours After Treatment	$\mu\text{g/ml}$ of $^{14}\text{C}$ Radioactivity Calculated as DCPD- $^{14}\text{C}$					
	Mice		Rats		Dogs	
	Blood	Plasma	Blood	Plasma	Blood	Plasma
1/4	1.48	2.48	-	-	-	-
1/2	-	-	-	-	4.11	11.17
1	5.51	9.83	-	-	5.82	29.70
2	4.91	11.36	10.65	11.51	6.31	39.95
4	3.75	8.21	11.92	14.44	5.83	35.95
6	2.53	4.96	19.76	23.28	5.07	33.20
24	0.24	0.36	14.09	15.47	3.21	11.62
48	0.08	0.06	1.93	2.13	1.32	3.07
72	<0.01	<0.01	0.47	0.36	0.24	1.24

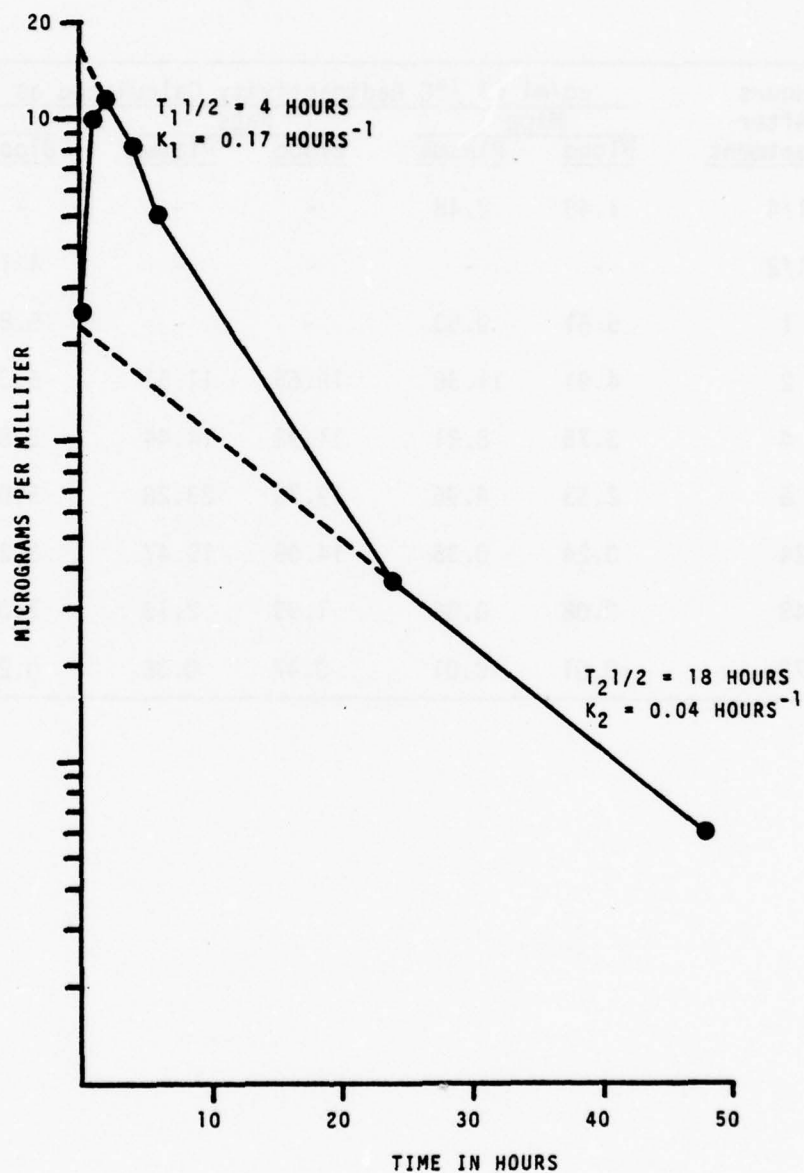


Figure II-L-4. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DCPD- $^{14}\text{C}$   $\mu\text{g/ml}$  in mice versus hours after administration of a single oral dose of 40 mg/kg of DCPD- $^{14}\text{C}$ .

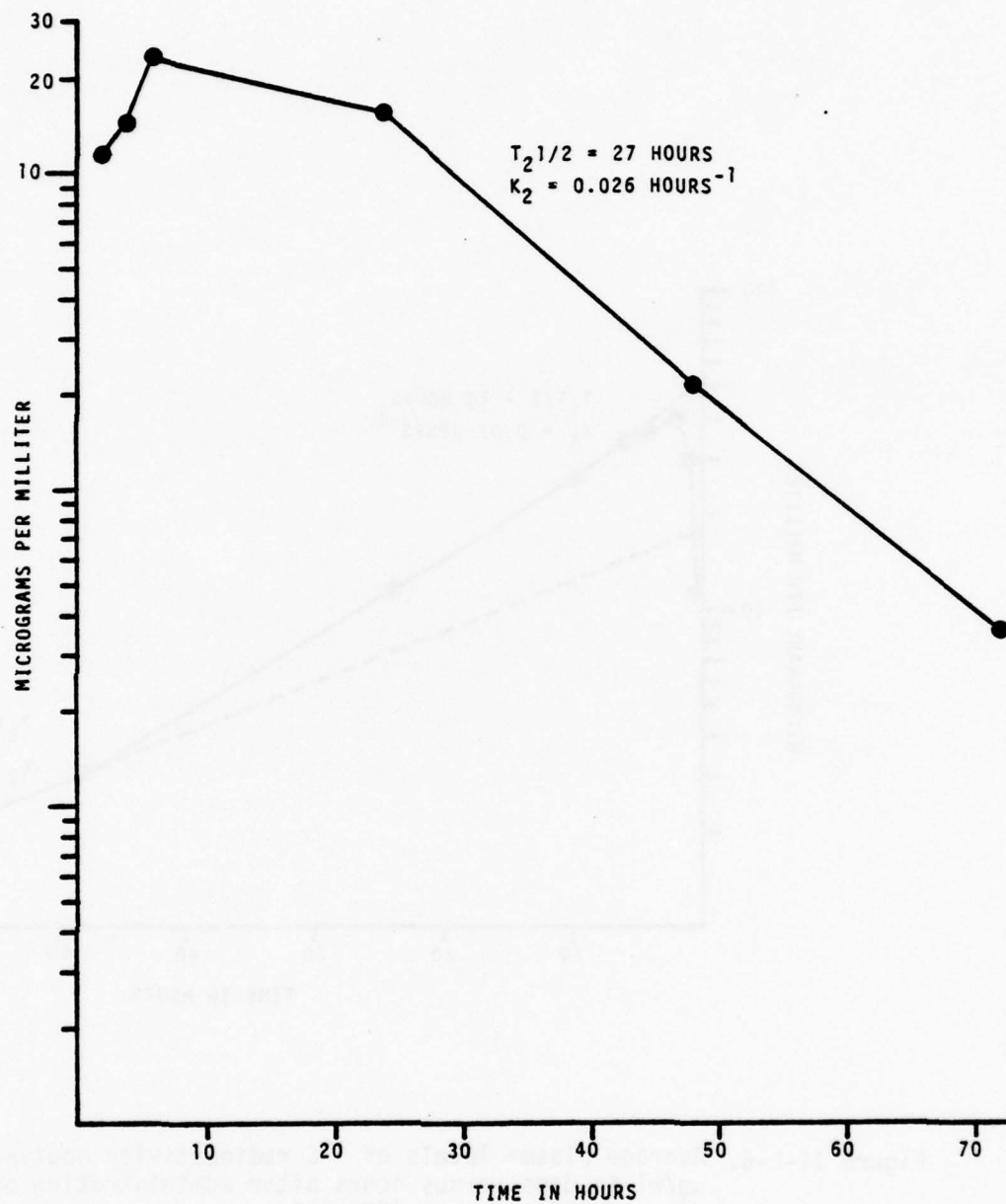


Figure II-L-5. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DCPD- $^{14}\text{C}$   $\mu\text{g/ml}$  in rats versus hours after administration of a single oral dose of 100 mg/kg of DCPD- $^{14}\text{C}$ .

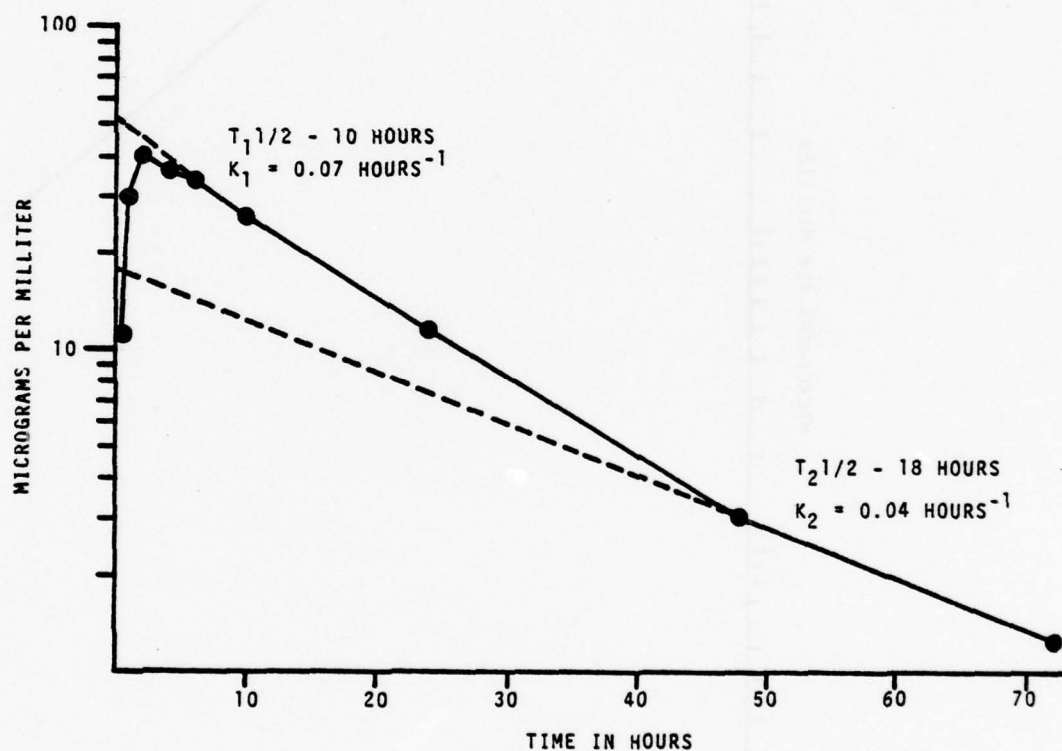


Figure II-L-6. Average plasma levels of  $^{14}\text{C}$  radioactivity equivalent of DCPD- $^{14}\text{C}$   $\mu\text{g}/\text{ml}$  in dogs versus hours after administration of a single oral dose of 100 mg/kg of DCPD- $^{14}\text{C}$ .

#### 4. RESULTS AND DISCUSSION (Continued)

##### B. Tissue Distribution in Mice

The results of the distribution of radioactivity in tissues of mice at various times after oral administration of DCPD-<sup>14</sup>C are shown in Table II-L-62. The radioactivity was widely distributed with high levels observed in all tissues at 1 and 2 hours after DCPD-<sup>14</sup>C administration. The highest levels were found in the urinary bladder, gall bladder, and fat. After six hours DCPD-<sup>14</sup>C levels declined rapidly in all tissues except the urinary bladder and fat. Still measurable amounts of radioactivity were detected in most of the tissues at 72 hours after administration of DCPD-<sup>14</sup>C. The highest levels found at 72 hours were in the liver. These results are in agreement with the absorption and half-life patterns shown in Figure II-L-4.

##### C. Tissue Distribution in Rats

The results of the distribution of radioactivity in tissues of rats at various times after administration of DCPD-<sup>14</sup>C are shown in Table II-L-63. The radioactivity was widely distributed with high levels found in all tissues at 1 and 2 hours. The highest levels were found in the fat, adrenals, and urinary bladder. At 24 hours levels were highest in the urinary bladder, liver, and kidneys. Radioactivity declined in all tissues except the urinary bladder after 24 hours, but the rate was slower in rat tissue than in mouse tissue. Radioactivity was detected in all tissues at 72 hours, and the highest level present at this time was in skin, liver, and kidneys. These results are consistent with the absorption and half-life patterns shown in Figure II-L-5.

##### D. Tissue Distribution in Dogs

The distribution of radioactivity in tissues of dogs at various times after administration of a single oral dose of DCPD-<sup>14</sup>C are presented in Table II-L-64. The radioactivity was widely distributed in all tissues, but the highest levels were found in bile, gall bladder, stomach, and urinary bladders at 4 hours after administration of DCPD-<sup>14</sup>C. At 24 hours, DCPD-<sup>14</sup>C levels were greatly reduced in all tissues with the highest amounts found in the bile and urinary bladder. At 7 days radioactivity was still detected in most tissues with the highest levels found in fat and liver. These results suggest the possibility of biliary excretion in dogs of DCPD-<sup>14</sup> derived compounds.

TABLE II-L-62

Tissue Distribution of  $^{14}\text{C}$  Radioactivity ( $\mu\text{g/g}$  or  $\text{ml}$ ) in Male Mice at Various Time Periods After Administration of a Single Oral Dose of 40  $\text{mg/kg}$  of DCPD- $^{14}\text{C}$

Tissue	$\mu\text{g}$ of $^{14}\text{C}$ Radioactivity Per Gram or $\text{ml}$ Wet Tissue Calculated as DCPD- $^{14}\text{C}$ *							
	15 min	1 hr	2 hrs	4 hrs	6 hrs	24 hrs	48 hrs	72 hrs
Spleen	2.02	8.85	8.30	6.71	3.44	0.16	0.11	0.15
Lungs	4.08	14.31	9.67	8.25	3.40	0.29	0.17	0.18
Heart	2.23	10.65	9.18	5.92	3.36	0.19	0.06	0.09
Liver	11.36	21.36	21.72	17.06	7.58	1.03	0.67	0.43
Kidneys	14.25	31.36	36.54	27.62	21.81	1.15	0.44	0.21
Testes	3.77	12.95	11.31	8.12	5.80	0.18	0.07	0.05
Brain	1.54	11.65	10.34	6.10	3.42	0.16	0.08	0.04
Abdominal Muscle	4.35	12.67	10.64	9.25	3.99	0.14	0.08	0.05
Fat	46.17	69.92	64.65	47.39	33.04	0.22	0.13	0.08
+Urinary Bladder	32.84	248.05	214.33	161.76	138.49	12.25	0.19	0.08
Adrenals	28.98	29.41	29.08	9.67	6.49	0.39	<0.01	<0.01
Eyes	0.88	8.72	7.16	9.05	4.42	0.46	0.05	0.08
Femur	1.53	6.77	6.25	6.07	3.27	0.36	0.05	0.05
Skin	6.69	12.70	10.09	9.99	7.50	1.53	0.82	0.19
+Gall Bladder	35.46	78.60	41.82	19.38	7.63	5.40	0.43	0.10
Spinal Cord	2.09	15.26	12.72	11.25	4.35	0.15	0.07	0.09

\*The values shown represent average of the organs of three mice at each time period.

+Without content

TABLE II-L-63

Tissue Distribution of  $^{14}\text{C}$  Radioactivity ( $\mu\text{g/g}$  or  $\text{ml}$ ) in Male Rats at Various Time Periods After Administration of a Single Oral Dose of 100  $\text{mg/kg}$  of DCPD- $^{14}\text{C}$

Tissue	$\mu\text{g}$ of $^{14}\text{C}$ Radioactivity Per Gram or $\text{ml}$ Wet Tissue Calculated as DCPD- $^{14}\text{C}$ *					
	2 hrs	4 hrs	6 hrs	24 hrs	48 hrs	72 hrs
Spleen	20.55	16.91	35.43	15.15	2.68	0.70
Lungs	29.71	25.84	34.11	16.05	2.38	0.82
Heart	23.40	17.34	32.28	13.82	1.32	0.62
Liver	75.30	45.04	67.40	74.42	11.32	1.94
Kidneys	61.27	64.20	80.13	70.74	18.74	1.72
Testes	18.08	18.44	31.98	12.87	1.92	0.73
Brain	25.37	18.24	32.36	12.25	1.76	0.60
Abdominal Muscle	25.36	15.75	30.20	12.79	3.93	0.57
Fat	180.60	134.12	366.03	20.42	3.36	1.12
†Urinary Bladder	75.15	120.52	127.50	113.14	65.79	1.14
Adrenals	91.07	49.36	153.76	27.00	2.69	1.40
Eyes	8.58	11.03	23.10	8.97	1.29	0.66
Femur	11.49	12.73	18.26	8.56	1.21	0.44
Skin	45.58	30.83	87.39	12.49	5.65	5.88

\*The values shown represent average of two rats at each time period.

†Without content.

TABLE II-L-64

Tissue Distribution of  $^{14}\text{C}$  Radioactivity ( $\mu\text{g}$  per gram or per ml) in Male Dogs at Various Time Periods After Administration of a Single Oral Dose of 100 mg/kg of DCPD- $^{14}\text{C}$

Tissue	$\mu\text{g}$ of $^{14}\text{C}$ Radioactivity Per Gram or ml Wet Tissue Calculated as DCPD- $^{14}\text{C}$				
	4 hrs	24 hrs	48 hrs	72 hrs	1 week
Spleen	9.35	6.09	0.96	0.48	0.51
Lungs	6.09	7.19	1.73	1.33	0.44
Heart	11.90	5.30	1.66	0.82	0.25
Liver	70.40	14.62	7.43	5.27	0.94
Kidneys*	44.78	14.30	3.08	2.67	0.53
Testes*	16.34	5.19	2.30	1.27	0.44
Medulla	5.76	3.09	2.80	0.87	0.46
Cerebrum	4.34	4.70	2.33	1.36	0.40
Cerebellum	5.09	1.75	0.55	1.24	0.45
Urinary Bladder**	171.48	44.40	20.46	4.54	0.44
Adrenals*	9.47	3.80	1.83	1.39	0.30
Eyes*	7.95	3.86	2.45	0.95	0.51
Femur*	3.45	2.08	2.20	1.81	0.69
Skin	15.71	23.32	5.42	4.32	0.41
Abdominal Muscle†	11.68	4.85	0.74	0.67	0.40
Bile	933.54	64.84	53.35	7.21	0.66
Fat	22.23	37.57	18.34	13.47	0.94
Thyroid	16.58	10.59	2.39	1.19	0.68
Lymph Nodes	17.41	6.74	3.55	1.03	0.79
Stomach**	157.58	2.93	2.08	1.70	0.40
Small Intestine**	40.49	3.87	2.28	0.86	0.25
Cecum**	32.79	<0.01	1.00	4.21	<0.01
Large Intestine**	25.47	2.67	1.62	1.14	<0.01
Gall Bladder	337.56	16.97	15.42	3.33	0.53
Bone Marrow	8.96	8.17	7.86	1.83	0.44
Spinal Cord	2.49	3.32	2.34	1.07	0.45
Pancreas	26.84	4.57	1.06	1.17	0.31

\*Value is average of two organs.

\*\*Tissue without content.

†Average of smooth and abdominal muscle values.

#### 4. RESULTS AND DISCUSSION (Continued)

##### D. Tissue Distribution in Dogs

The distribution of radioactivity in various sections of the individual eyes of dogs is summarized in Table II-L-65. These results show that the highest concentration of radioactivity was located in the whole eye (all parts) at 4 hours after administration of DCPD- $^{14}\text{C}$ . After that time radioactivity was greatly reduced. At 72 hours radioactivity decreased at a steady rate, but it was still detected in all sections of the eye at 7 days.

##### E. Percentage of Excretion

The percentage of radioactivity recovered in urine, feces, the gastrointestinal tract, expired air, and the carcass of mice and rats is presented in Tables II-L-66 and II-L-67, respectively. Similar data from dogs also including the percentage of radioactivity recovered in excised organs, bile, blood, and muscle are given in Table II-L-68. The primary route of excretion of DCPD- $^{14}\text{C}$  (or metabolites) appears to be through the urine in all three species.

Marked differences did occur in the rate of excretion of  $^{14}\text{C}$  in urine with mice reaching maximum excretion at 24 hours and rats and dogs at 72 hours. Approximately 85% of all radioactivity was recovered from urine and feces of mice and dogs within 24 hours after a single oral dose of DCPD- $^{14}\text{C}$ . Small amounts of  $^{14}\text{C}$  were also detected in the expired air from rats, but the amount found from mice was higher than expected. The exact nature of this component was not determined; however, this route of excretion cannot be considered as the major metabolic pathway.

##### F. Metabolic Fate of DCPD- $^{14}\text{C}$ in Mice, Rats, and Dogs

The 0- to 24-hour urines from mice, rats, and dogs were analyzed by thin-layer chromatography (TLC). The results of the initial TLC analyses are shown in Table II-L-69. Urine from mice and dogs showed two radioactive components while the rat urine showed three components. The major component present in all three species, designated as I, contained 60 to 95% of the radioactivity and did not move from the origin. The other components with varying polarity had Rf values of: Mouse II, Rf = 0.27 (5.4%); Rat II, Rf = 0.33 (22.7%) and III Rf = 0.49 (18.2%); Dog II, Rf = 0.26 (5.0%). The Rf value of DCPD- $^{14}\text{C}$  under identical conditions was found to be 0.65. The 0- to 24-hour urines from

TABLE 11-L-65  
Distribution of  $^{14}\text{C}$  Radioactivity in Various Sections of Individual Eyes of Male  
Dogs After Administration of a Single Oral Dose of 100 mg/kg of DCPD- $^{14}\text{C}$

Kill Time	Eye Tissue Section	$\mu\text{g/g}$	Section Weight g	$\mu\text{g/Section}$	$\mu\text{g/g for Whole Eye}$	Total $\mu\text{g/Eye}$	% Dose/Organ
Dog No. 7 4 hrs	Right: Cornea	10.86	0.08	0.88			
	Lens	2.49	0.29	0.72			
	Fluid	8.77	3.24	28.41	7.97	41.31	<0.01
	Ocular Tissue	9.74	1.16	11.30			
	Left: Cornea	11.06	0.06	0.66			
	Lens	2.61	0.25	0.65			
Dog No. 8 24 hrs	Fluid	8.44	3.00	25.32	7.92	37.91	<0.01
	Ocular Tissue	9.56	1.18	11.28			
	Right: Cornea	<0.01	1.00	<0.01			
	Lens	2.55	0.37	0.94	4.14	20.14	<0.01
	Fluid	6.37	2.42	15.42			
	Ocular Tissue	3.63	1.04	3.78			
Dog No. 9 48 hrs.	Left: Cornea	<0.01	1.00	<0.01			
	Lens	<0.01	0.27	<0.01	3.58	17.31	<0.01
	Fluid	6.09	2.01	12.25			
	Ocular Tissue	3.72	1.36	5.06			
	Right: Cornea	2.08	0.13	0.27			
	Lens	1.67	0.44	0.73	2.22	13.32	<0.01
Dog No. 10 72 hrs.	Fluid	3.22	3.07	9.89			
	Ocular Tissue	1.90	1.28	2.43			
	Left: Cornea	2.13	0.13	0.28			
	Lens	2.52	0.39	0.98	2.09	10.67	<0.01
	Fluid	3.10	2.80	8.68			
	Ocular Tissue	0.62	1.19	0.73			
Dog No. 11 7 days	Right: Cornea	1.16	0.05	0.06			
	Lens	1.03	0.25	0.26	1.02	4.28	<0.01
	Fluid	1.08	2.85	3.08			
	Ocular Tissue	0.79	1.11	0.88			
	Left: Cornea	0.26	0.35	0.09			
	Lens	1.33	0.04	0.05	0.89	4.04	<0.01
Dog No. 11 7 days	Fluid	1.05	2.79	2.93			
	Ocular Tissue	0.90	1.08	0.97			
	Right: Cornea	0.27	0.12	0.03			
	Lens	0.57	0.38	0.22	0.35	1.17	<0.01
	Fluid	0.25	2.15	0.54			
	Ocular Tissue	0.31	1.21	0.38			
Dog No. 11 7 days	Left: Cornea	0.45	0.11	0.05			
	Lens	0.52	0.39	0.20	0.40	1.50	<0.01
	Fluid	0.27	3.06	0.83			
	Ocular Tissue	0.35	1.21	0.42			
	Right: Cornea	0.27	0.12	0.03			
	Lens	0.57	0.38	0.22	0.35	1.17	<0.01

TABLE II-L-66

Percent of  $^{14}\text{C}$  Radioactivity Recovered in Urine, Feces, Carcass,  
Gastrointestinal Tract and Expired Air by Mice at Various Time  
Periods After Administration of a Single Oral Dose of  
40 mg/kg of DCPD- $^{14}\text{C}$

Time in Hours	% $^{14}\text{C}$ Radioactivity Recovered*					Total
	Urine	Feces	Carcass	GI Tract	Expired Air	
0-15 min	<0.01	<0.01	7.3	33.13	none	40.43
0-1 hr	9.66	0.48	26.26	43.06	0.17	80.17
0-2 hrs	14.71	none	16.19	14.28	1.29	46.47
0-4 hrs	24.63	3.96	17.16	17.13	3.95	67.28
0-6 hrs	36.70	36.20	10.09	7.43	5.32	95.74
0-24 hrs	75.42	10.17	1.40	2.09	6.15	95.23
0-48 hrs	70.09	16.89	0.78	0.28	3.59	91.63
0-72 hrs	34.41†	19.03	0.27	0.09	2.45	56.25

†Appear to be lost from urine.

\*Low recoveries are due to the volatility of the DCPD.

TABLE II-L-67

Percent of  $^{14}\text{C}$  Radioactivity Recovered in Urine, Feces, Carcass,  
Gastrointestinal Tract and Expired Air by Rats at Various Time  
Periods After Administration of a Single Oral Dose of  
100 mg/kg of DCPD- $^{14}\text{C}$

Time in Hours	% $^{14}\text{C}$ Radioactivity Recovered*					Total
	Urine	Feces	Carcass	GI Tract	Expired Air	
0-2 hrs	4.48	0.19	14.14	35.04	<0.01	53.85
0-4 hrs	2.10	0.87	22.82	33.95	0.54	60.28
0-6 hrs	8.70	0.44	31.65	34.06	0.25	75.10
0-24 hrs	53.71	15.17	12.61	27.35	0.10	108.94
0-48 hrs	39.20	28.21	3.30	5.42	0.34	76.47
0-72 hrs	74.89	15.01	1.78	0.35	2.46	94.49

\*The values shown represent average of two rats at each time period.

TABLE II-L-63

Percent of  $^{14}\text{C}$  Radioactivity Recovered From Male Dogs at Various Time Periods  
After Administration of a Single Oral Dose of 100 mg/kg of DCPD- $^{14}\text{C}$

Percent <sup>14</sup> C Radioactivity Recovered Calculated as DCPD- <sup>14</sup> C									
Dog No.	Time In Hours	Urine	Feces	GI Tract Contents and Tissue	Excised Organs	Bile	* Blood	** Muscle	Total
11	4 hrs	16.90	1.27	19.71	4.09	0.72 (5.84)	0.54	3.50	46.73
8	24 hrs	64.54	3.83	0.91	0.90	0.04 (5.23)	0.28	1.45	71.95
9	48 hrs	77.96	7.59	0.32	0.38	0.03 (5.73)	0.12	0.22	86.62
10	72 hrs	80.84	4.13	0.06	0.23	0.01 (6.43)	0.02	0.22	85.51
7	1 wk	66.73	3.65	0.02	0.05	<0.01 (5.32)	0.05	0.12	70.63
Body Weights and Administered Dose - 11									
			8	7.6 kg	760 mgs				
			9	8.3 kg	830 mgs				
			10	8.9 kg	890 mgs				
			7	8.8 kg	880 mgs				
				8.6 kg	860 mgs				

\*Blood values are calculated as 9% of the body weight.

\*\*Muscle values are calculated as 30% of the body weight.

( ) Values in parentheses indicate weights of bile in grams.

TABLE II-L-69

Percent  $^{14}\text{C}$  Radioactivity Associated With Different Components Resolved  
by Thin-Layer Chromatography of 0-24 Hour Urine From Mouse,  
Rat, and Dog After Administration of a Single Oral  
Dose of 40 mg or 100 mg/kg of DCPD- $^{14}\text{C}$

Sample	Component	Rf	% Radioactivity In Each Component
DCPD- $^{14}\text{C}$	DCPD- $^{14}\text{C}$ Trailing	0.65	100.00
0-24 Hour Mouse Urine	I	0.00	94.60
	II	0.27	5.40
0-24 Hour Rat Urine	I	0.04	59.10
	II	0.33	22.70
	III	0.49	18.20
0-24 Hour Dog Urine	I	0.00	95.00
	II	0.26	5.00

Developing solvent system: Ethylacetate:Methanol (9:1 v/v).

#### 4. RESULTS AND DISCUSSION (Continued)

##### F. Metabolic Fate of DCPD-<sup>14</sup>C in Mice, Rats, and Dogs (Continued)

mice, rats, dogs, and control urine spiked with DCPD-<sup>14</sup>C were extracted with DEE at pH = 6-7, and these data are shown in Table II-L-70. Approximately 1 to 3% of the total radioactivity was extracted into DEE from urine of all three species, whereas DCPD-<sup>14</sup>C was 100% extractable into DEE from control urine spiked with DCPD-<sup>14</sup>C. These results indicate the presence of 1 to 3% nonmetabolized DCPD-<sup>14</sup>C in the urine of all three species with a high percentage of other metabolites.

The 0- to 24-hour urines from mice, rats, dogs, and a control urine spiked with DCPD-<sup>14</sup>C were subjected to enzymatic hydrolysis with glucuronidase and then extracted with DEE. The data relating to the percent of radioactivity extractable into DEE are summarized in Table II-L-71. The results show that the radioactivity extracted into DEE increased following enzyme treatment in all three species, and the highest levels were in rat and dog urine. Therefore, enzymatic hydrolysis of the urine samples with  $\beta$ -glucuronidase or sulfatase did occur indicating the presence of urine conjugates. These results further indicate that glucuronidase reacted with DCPD-<sup>14</sup>C altering its solubility in DEE.

In order to achieve complete resolution of radioactive components, urine samples, extracted urine, and DEE extracts were subjected to TLC and these results are shown in Table II-L-72. The urine from mice and rats showed seven different components while the dog urine had six. Furthermore, these components had similar R<sub>f</sub> values indicating common metabolites in all three species. The experiments were performed similarly for 0- to 24-hour urines spiked with DCPD-<sup>14</sup>C. The results of these analyses showed that none of three components corresponded to urines spiked with DCPD-<sup>14</sup>C.

#### 5. LITERATURE CITED

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TABLE II-L-70

Percent  $^{14}\text{C}$  Radioactivity Extracted Into Diethyl ether From 0-24 Hour  
Urine From Mouse, Rat, and Dog After Administration of a Single  
Oral Dose of 40 mg or 100 mg/kg of DCPD- $^{14}\text{C}$

Sample	% $^{14}\text{C}$ Extracted into DEE	% $^{14}\text{C}$ Remaining in Urine	Total % $^{14}\text{C}$ Recovery
DEE Control (Rat) Urine Spiked with DCPD- $^{14}\text{C}$	105.00	4.00	109.00
DEE 0-24 hr Mouse Urine	2.80	84.20	87.00
DEE 0-24 hr Rat Urine	1.00	98.60	99.60
DEE 0-24 hr Dog Urine	1.70	85.70	87.40

DEE = Diethyl ether.

TABLE II-L-71

Percent of  $^{14}\text{C}$  Radioactivity Extracted into Diethyl ether from Urine  
Treated with Glusulase For 0-24 Hour Period From Mouse, Rat,  
and Dog, After Administration of a Single Oral Dose of  
40 mg or 100 mg/kg of DCPD- $^{14}\text{C}$

Sample	% $^{14}\text{C}$ Extracted into DEE	% $^{14}\text{C}$ Remaining in Urine	Total % $^{14}\text{C}$ Recovery
DEE Control Urine Spiked with DCPD- $^{14}\text{C}$ and Glusulase	8.00	93.16	101.16
DEE Extract 0-24- Hour Mouse Urine and Glusulase	5.50	89.90	95.10
DEE Extract 0-24- Hour Rat Urine and Glusulase	36.40	63.70	100.10
DEE Extract 0-24- Hour Dog Urine and Glusulase	19.20	71.70	90.90

DEE = Diethyl ether

Glusulase =  $\beta$ -glucuronidase + sulfatase

TABLE II-L-72

Percent  $^{14}\text{C}$  Radioactivity in Various Components Resolved by Thin-Layer Chromatography of 0-24 Hour Whole Urine, Extracted Urine, DEE Extract of Mouse, Rat, and Dog After Administration of 40 mg/kg (Mouse) and 100 mg/kg (Rat and Dog) of DCPD- $^{14}\text{C}$

Components	Rf*	RAT			MOUSE			DOG		
		% $^{14}\text{C}$ Whole Urine	% $^{14}\text{C}$ **Ext. Urine	% $^{14}\text{C}$ DEE Extract	% $^{14}\text{C}$ Whole Urine	% $^{14}\text{C}$ Ext. Urine	% $^{14}\text{C}$ DEE Extract	% $^{14}\text{C}$ Whole Urine	% $^{14}\text{C}$ Ext. Urine	% $^{14}\text{C}$ DEE Extract
I	0.00	41.10	41.10	0.00	55.80	55.80	0.00	81.26	81.30	0.00
II	0.26	19.70	16.40	3.30	2.20	2.20	0.00	5.80	3.90	1.90
III	0.33	2.70	1.40	1.30	1.60	1.40	0.20	1.50	0.30	1.20
IV	0.44	5.00	2.90	2.10	4.70	2.20	2.50	0.00	0.00	0.00
V	0.50	22.30	5.90	16.40	24.60	7.50	17.20	6.30	0.40	5.90
VI	0.56	6.30	0.40	5.90	10.10	0.80	9.30	4.00	0.10	3.90
VII	0.60	3.00	0.00	3.00	1.10	0.20	0.90	1.20	0.00	1.20
Total % Radio Activity Accounted		100.00	68.10	31.90	100.00	69.90	30.60	100.00	85.90	14.10

\*Developing solvent system: Ethylacetate:Methanol (9:1 v/v).

\*\*Urine left over after extraction with DEE.

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